```
L18             QUE  SPE=ON  ABB=ON  PLU=ON  PROTEIN
L19             QUE  SPE=ON  ABB=ON  PLU=ON  GWT1 OR (GWT(1W)(1 OR I)) OR
                 GWTI
L20             QUE  SPE=ON  ABB=ON  PLU=ON  GENE
L21             QUE  SPE=ON  ABB=ON  PLU=ON  SACCHAROMYC? OR CEREVIS?
L22             QUE  SPE=ON  ABB=ON  PLU=ON  TEST OR TESTING OR TESTED OR
                 DETECT? OR DETERMIN? OR ANALY? OR SENSE OR SENSED OR SEN
                SING OR BIOSENS? OR ?ASSAY? OR ?MEASUR?
L23             QUE  SPE=ON  ABB=ON  PLU=ON  ANCHOR?
L24             QUE  SPE=ON  ABB=ON  PLU=ON  GPI
L25             QUE  SPE=ON  ABB=ON  PLU=ON  PI
L26             QUE  SPE=ON  ABB=ON  PLU=ON  ?GLYCOS? OR GLC?
L27             QUE  SPE=ON  ABB=ON  PLU=ON  ?PHOSPHATID?
L28             QUE  SPE=ON  ABB=ON  PLU=ON  ?INOSIT?
L29             QUE  SPE=ON  ABB=ON  PLU=ON  (?PHOSPHATID? (1T)?INOSIT?)
                OR (?PHOSPHATID? (1W)?INOSIT?)
L30             QUE  SPE=ON  ABB=ON  PLU=ON  N(1W)ACYL?
L31             QUE  SPE=ON  ABB=ON  PLU=ON  ACYLAT?
L32             QUE  SPE=ON  ABB=ON  PLU=ON  THIN(1W)LAYER
L33             QUE  SPE=ON  ABB=ON  PLU=ON  CHROMATOG?
L34             QUE  SPE=ON  ABB=ON  PLU=ON  TLC
L35             QUE  SPE=ON  ABB=ON  PLU=ON  CELL(2A)(WALL OR SURFACE)
L68        2681 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L13 (7A)(L19 OR (L24 OR
                L25) OR L29)
L69         209 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L68 AND L3
L70         418 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L68 (15A)(L16 OR L22)
L71         552 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  (L69 OR L70)
L72          10 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L71 AND (L19 OR L21)
L73         102 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L68 AND ((L13(5A)L24) OR
                L15)
L74           7 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L73 AND  (L19 OR L21)
L75          12 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L72 OR L74
L76          12 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L75 AND (L13 OR L14 OR
                L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR
                L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR
                L33 OR L34 OR L35)
L77          12 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  (L75 OR L76)
L78           6 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L77 AND (L6 OR L7 OR L8
                OR L9 OR L10 OR L11 OR L12)
L79           6 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L77 NOT L78


=> d que l97
L6              QUE  SPE=ON  ABB=ON  PLU=ON  TSUKAHARA, K?/AU,AUTH
L7              QUE  SPE=ON  ABB=ON  PLU=ON  TSUCHIYA, M?/AU,AUTH
L8              QUE  SPE=ON  ABB=ON  PLU=ON  JIGAMI, Y?/AU,AUTH
L9              QUE  SPE=ON  ABB=ON  PLU=ON  NAKAYAMA, K?/AU,AUTH
L10             QUE  SPE=ON  ABB=ON  PLU=ON  UMEMURA, M?/AU,AUTH
L11             QUE  SPE=ON  ABB=ON  PLU=ON  OKAMOTO, M?/AU,AUTH
L12             QUE  SPE=ON  ABB=ON  PLU=ON  EISAI/CS,SO,PA OR ((NATIONAL
                 (1W)(INST OR INSTITUTE))(5A)(ADVANCED(1W)INDUSTRIAL)(5A)
                (SCIENCE (3W)(TECH OR TECHNOL OR TECHNOLOGY)))/CS,SO,PA
L14             QUE  SPE=ON  ABB=ON  PLU=ON  FUNGUS OR FUNGI OR FUNGAL?
L15             QUE  SPE=ON  ABB=ON  PLU=ON  ANTIFUNG? OR FUNGICID? OR FU
                NGISTAT?
L16             QUE  SPE=ON  ABB=ON  PLU=ON  SCREEN? OR TEST OR TESTING O
                R TESTED OR EVALUAT? OR DETERMIN?
L19             QUE  SPE=ON  ABB=ON  PLU=ON  GWT1 OR (GWT(1W)(1 OR I)) OR
                 GWTI
L21             QUE  SPE=ON  ABB=ON  PLU=ON  SACCHAROMYC? OR CEREVIS?
```

```
L22             QUE  SPE=ON  ABB=ON  PLU=ON  TEST OR TESTING OR TESTED OR
                 DETECT? OR DETERMIN? OR ANALY? OR SENSE OR SENSED OR SEN
                SING OR BIOSENS? OR ?ASSAY? OR ?MEASUR?
L24             QUE  SPE=ON  ABB=ON  PLU=ON  GPI
L25             QUE  SPE=ON  ABB=ON  PLU=ON  PI
L29             QUE  SPE=ON  ABB=ON  PLU=ON  (?PHOSPHATID? (1T)?INOSIT?)
                OR (?PHOSPHATID? (1W)?INOSIT?)
L30             QUE  SPE=ON  ABB=ON  PLU=ON  N(1W)ACYL?
L31             QUE  SPE=ON  ABB=ON  PLU=ON  ACYLAT?
L33             QUE  SPE=ON  ABB=ON  PLU=ON  CHROMATOG?
L34             QUE  SPE=ON  ABB=ON  PLU=ON  TLC
L35             QUE  SPE=ON  ABB=ON  PLU=ON  CELL(2A)(WALL OR SURFACE)
L43          41 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  (GWT1/CNS OR
                (GWT/CNS(1W)(1/CNS OR I/CNS)) OR GWTI/CNS)
L81           0 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L43
L82             QUE  SPE=ON  ABB=ON  PLU=ON  "SACCHAROMYCES CEREVISIAE PR
                OTEINS"+PFT,OLD,NEW,NT/CT
L83        1958 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  (L82 OR L21) AND (L19
                OR (L24 OR L25) OR L29)
L84             QUE  SPE=ON  ABB=ON  PLU=ON  "ANTIFUNGAL AGENTS"+PFT,OLD,
                NEW/CT
L85             QUE  SPE=ON  ABB=ON  PLU=ON  "DRUG EVALUATION, PRECLINICA
                L"+PFT,OLD,NEW,NT/CT
L86        1958 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L81 OR L83
L87          14 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L86 AND (L82(L)AN/CT)

L88        1386 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L86 AND (L84 OR L85
                OR L16 OR L22 OR L33 OR L35 OR (L30 OR L31))
L89          11 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L88 AND L85
L90         591 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L88 AND (L84 OR (L14
                OR L15))
L91         524 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L90 AND (L85 OR L16
                OR L22 OR (L33 OR L34))
L92           5 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L91 AND (L30 OR L31)
L93         122 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L91 AND L35
L94          30 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L87 OR L89 OR L92
L95           6 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L93 AND L94
L96           1 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L95 AND (L6 OR L7 OR
                L8 OR L9 OR L10 OR L11 OR L12)
L97           5 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L95 NOT L96


=> d que l113
L6              QUE  SPE=ON  ABB=ON  PLU=ON  TSUKAHARA, K?/AU,AUTH
L7              QUE  SPE=ON  ABB=ON  PLU=ON  TSUCHIYA, M?/AU,AUTH
L8              QUE  SPE=ON  ABB=ON  PLU=ON  JIGAMI, Y?/AU,AUTH
L9              QUE  SPE=ON  ABB=ON  PLU=ON  NAKAYAMA, K?/AU,AUTH
L10             QUE  SPE=ON  ABB=ON  PLU=ON  UMEMURA, M?/AU,AUTH
L11             QUE  SPE=ON  ABB=ON  PLU=ON  OKAMOTO, M?/AU,AUTH
L12             QUE  SPE=ON  ABB=ON  PLU=ON  EISAI/CS,SO,PA OR ((NATIONAL
                 (1W)(INST OR INSTITUTE))(5A)(ADVANCED(1W)INDUSTRIAL)(5A)
                (SCIENCE (3W)(TECH OR TECHNOL OR TECHNOLOGY)))/CS,SO,PA
L13             QUE  SPE=ON  ABB=ON  PLU=ON  ANTAGON? OR INHIBIT? OR PROH
                IBIT? OR PREVENT? OR DIMINISH? OR REDUC? OR IMPED? OR DEP
                RESS? OR SUPPRESS? OR REPRESS? OR OBSTRUCT? OR RESTRICT?
                OR TERMINAT? OR BLOCK? OR STOP? OR RETARD? OR SLOW? OR DE
                LAY? OR LIMIT? OR DECREAS? OR LOWER? OR LESSEN? OR MINIMI
                Z? OR MINIMIS? OR DISRUPT?
L14             QUE  SPE=ON  ABB=ON  PLU=ON  FUNGUS OR FUNGI OR FUNGAL?
L15             QUE  SPE=ON  ABB=ON  PLU=ON  ANTIFUNG? OR FUNGICID? OR FU
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```
                NGISTAT?
L16             QUE  SPE=ON  ABB=ON  PLU=ON  SCREEN? OR TEST OR TESTING O
                R TESTED OR EVALUAT? OR DETERMIN?
L17             QUE  SPE=ON  ABB=ON  PLU=ON  OVEREXPRESS? OR (OVER(1W)EXP
                RESS?)
L18             QUE  SPE=ON  ABB=ON  PLU=ON  PROTEIN
L19             QUE  SPE=ON  ABB=ON  PLU=ON  GWT1 OR (GWT(1W)(1 OR I)) OR
                 GWTI
L20             QUE  SPE=ON  ABB=ON  PLU=ON  GENE
L21             QUE  SPE=ON  ABB=ON  PLU=ON  SACCHAROMYC? OR CEREVIS?
L22             QUE  SPE=ON  ABB=ON  PLU=ON  TEST OR TESTING OR TESTED OR
                 DETECT? OR DETERMIN? OR ANALY? OR SENSE OR SENSED OR SEN
                SING OR BIOSENS? OR ?ASSAY? OR ?MEASUR?
L23             QUE  SPE=ON  ABB=ON  PLU=ON  ANCHOR?
L24             QUE  SPE=ON  ABB=ON  PLU=ON  GPI
L25             QUE  SPE=ON  ABB=ON  PLU=ON  PI
L26             QUE  SPE=ON  ABB=ON  PLU=ON  ?GLYCOS? OR GLC?
L27             QUE  SPE=ON  ABB=ON  PLU=ON  ?PHOSPHATID?
L28             QUE  SPE=ON  ABB=ON  PLU=ON  ?INOSIT?
L29             QUE  SPE=ON  ABB=ON  PLU=ON  (?PHOSPHATID? (1T)?INOSIT?)
                OR (?PHOSPHATID? (1W)?INOSIT?)
L30             QUE  SPE=ON  ABB=ON  PLU=ON  N(1W)ACYL?
L31             QUE  SPE=ON  ABB=ON  PLU=ON  ACYLAT?
L32             QUE  SPE=ON  ABB=ON  PLU=ON  THIN(1W)LAYER
L33             QUE  SPE=ON  ABB=ON  PLU=ON  CHROMATOG?
L34             QUE  SPE=ON  ABB=ON  PLU=ON  TLC
L35             QUE  SPE=ON  ABB=ON  PLU=ON  CELL(2A)(WALL OR SURFACE)
L43              41 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  (GWT1/CNS OR
                (GWT/CNS(1W)(1/CNS OR I/CNS)) OR GWTI/CNS)
L98             QUE  SPE=ON  ABB=ON  PLU=ON  "GWT1 GENE"+PFT,OLD,NEW,NT/C
                T
L99              1 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  L43 OR L98
L100            QUE  SPE=ON  ABB=ON  PLU=ON  "SACCHAROMYCES CEREVISIAE PR
                OTEIN"+PFT,OLD,NEW,NT/CT
L101             5 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  GWT1 OR (GWT(1W)(1 OR
                I)) OR GWTI
L102          1013 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  (L100 OR L21) AND
                ((L24 OR L25) OR L29)
L103          1015 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  L99 OR (L101 OR L102)
L104            QUE  SPE=ON  ABB=ON  PLU=ON  "ANTIFUNGAL ACTIVITY"+PFT,OL
                D,NEW,NT/CT
L105            QUE  SPE=ON  ABB=ON  PLU=ON  "ANTIFUNGAL AGENT"+PFT,OLD,N
                EW,NT/CT
L106            QUE  SPE=ON  ABB=ON  PLU=ON  "DRUG SCREENING"+PFT,OLD,NEW
                ,NT/CT
L107             674 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  L103 AND (L106 OR L16
                OR L22 OR (L33 OR L34))
L108             263 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  L107 AND ((L14 OR L15)
                OR (L104 OR L105))
L109              28 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  L108 AND ((L104 OR
                L105) OR L15)
L110              28 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  L109 AND (L13 OR L14
                OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23
                OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32
                OR L33 OR L34 OR L35)
L111              28 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  (L109 OR L110)
L112               2 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  L111 AND (L6 OR L7 OR
                L8 OR L9 OR L10 OR L11 OR L12)
L113              26 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  L111 NOT L112
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```
=> d his l126

     (FILE 'BIOSIS, CABA, BIOTECHNO, DRUGU, VETU' ENTERED AT 13:07:01 ON 11
     SEP 2009)
L126         12 S L124 NOT L125

=> d que l126
L6              QUE  SPE=ON  ABB=ON  PLU=ON  TSUKAHARA, K?/AU,AUTH
L7              QUE  SPE=ON  ABB=ON  PLU=ON  TSUCHIYA, M?/AU,AUTH
L8              QUE  SPE=ON  ABB=ON  PLU=ON  JIGAMI, Y?/AU,AUTH
L9              QUE  SPE=ON  ABB=ON  PLU=ON  NAKAYAMA, K?/AU,AUTH
L10             QUE  SPE=ON  ABB=ON  PLU=ON  UMEMURA, M?/AU,AUTH
L11             QUE  SPE=ON  ABB=ON  PLU=ON  OKAMOTO, M?/AU,AUTH
L12             QUE  SPE=ON  ABB=ON  PLU=ON  EISAI/CS,SO,PA OR ((NATIONAL
                 (1W)(INST OR INSTITUTE))(5A)(ADVANCED(1W)INDUSTRIAL)(5A)
                (SCIENCE (3W)(TECH OR TECHNOL OR TECHNOLOGY)))/CS,SO,PA
L13             QUE  SPE=ON  ABB=ON  PLU=ON  ANTAGON? OR INHIBIT? OR PROH
                IBIT? OR PREVENT? OR DIMINISH? OR REDUC? OR IMPED? OR DEP
                RESS? OR SUPPRESS? OR REPRESS? OR OBSTRUCT? OR RESTRICT?
                OR TERMINAT? OR BLOCK? OR STOP? OR RETARD? OR SLOW? OR DE
                LAY? OR LIMIT? OR DECREAS? OR LOWER? OR LESSEN? OR MINIMI
                Z? OR MINIMIS? OR DISRUPT?
L14             QUE  SPE=ON  ABB=ON  PLU=ON  FUNGUS OR FUNGI OR FUNGAL?
L15             QUE  SPE=ON  ABB=ON  PLU=ON  ANTIFUNG? OR FUNGICID? OR FU
                NGISTAT?
L16             QUE  SPE=ON  ABB=ON  PLU=ON  SCREEN? OR TEST OR TESTING O
                R TESTED OR EVALUAT? OR DETERMIN?
L17             QUE  SPE=ON  ABB=ON  PLU=ON  OVEREXPRESS? OR (OVER(1W)EXP
                RESS?)
L18             QUE  SPE=ON  ABB=ON  PLU=ON  PROTEIN
L19             QUE  SPE=ON  ABB=ON  PLU=ON  GWT1 OR (GWT(1W)(1 OR I)) OR
                 GWTI
L20             QUE  SPE=ON  ABB=ON  PLU=ON  GENE
L21             QUE  SPE=ON  ABB=ON  PLU=ON  SACCHAROMYC? OR CEREVIS?
L22             QUE  SPE=ON  ABB=ON  PLU=ON  TEST OR TESTING OR TESTED OR
                 DETECT? OR DETERMIN? OR ANALY? OR SENSE OR SENSED OR SEN
                SING OR BIOSENS? OR ?ASSAY? OR ?MEASUR?
L23             QUE  SPE=ON  ABB=ON  PLU=ON  ANCHOR?
L24             QUE  SPE=ON  ABB=ON  PLU=ON  GPI
L25             QUE  SPE=ON  ABB=ON  PLU=ON  PI
L26             QUE  SPE=ON  ABB=ON  PLU=ON  ?GLYCOS? OR GLC?
L27             QUE  SPE=ON  ABB=ON  PLU=ON  ?PHOSPHATID?
L28             QUE  SPE=ON  ABB=ON  PLU=ON  ?INOSIT?
L29             QUE  SPE=ON  ABB=ON  PLU=ON  (?PHOSPHATID? (1T)?INOSIT?)
                OR (?PHOSPHATID? (1W)?INOSIT?)
L30             QUE  SPE=ON  ABB=ON  PLU=ON  N(1W)ACYL?
L31             QUE  SPE=ON  ABB=ON  PLU=ON  ACYLAT?
L32             QUE  SPE=ON  ABB=ON  PLU=ON  THIN(1W)LAYER
L33             QUE  SPE=ON  ABB=ON  PLU=ON  CHROMATOG?
L34             QUE  SPE=ON  ABB=ON  PLU=ON  TLC
L35             QUE  SPE=ON  ABB=ON  PLU=ON  CELL(2A)(WALL OR SURFACE)
L43          41 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  (GWT1/CNS OR
                (GWT/CNS(1W)(1/CNS OR I/CNS)) OR GWTI/CNS)
L114          0 SEA L43
L115         16 SEA L19
L116       2297 SEA L21 AND ((L24 OR L25) OR L29)
L117       2306 SEA (L114 OR L115 OR L116)
L118       1418 SEA L117 AND (L16 OR L22 OR (L33 OR L34))
L119         54 SEA L118 AND (L15 OR (L13(5A) L14))
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L120          6 SEA L119 AND (L33 OR L34)
L121          6 SEA L119 AND ((L16 OR L22)(7A)(L15 OR (L13(5A) L14)))
L122         12 SEA L120 OR L121
L123         12 SEA L122 AND (L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR
                L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR
                L29 OR L30 OR L31 OR L32 OR L33 OR L34 OR L35)
L124         12 SEA (L122 OR L123)
L125          0 SEA L124 AND (L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12)
L126         12 SEA L124 NOT L125


=> d his l132

     (FILE 'PASCAL, JAPIO, LIFESCI, CEABA-VTB, BIOENG, BIOTECHDS, DRUGB, VETB,
     SCISEARCH, CONFSCI, DISSABS, RDISCLOSURE' ENTERED AT 13:15:09 ON 11 SEP
     2009)
L132         26 S L130 NOT L131

     FILE 'STNGUIDE' ENTERED AT 13:21:45 ON 11 SEP 2009

=> d que l132
L6               QUE  SPE=ON  ABB=ON  PLU=ON  TSUKAHARA, K?/AU,AUTH
L7               QUE  SPE=ON  ABB=ON  PLU=ON  TSUCHIYA, M?/AU,AUTH
L8               QUE  SPE=ON  ABB=ON  PLU=ON  JIGAMI, Y?/AU,AUTH
L9               QUE  SPE=ON  ABB=ON  PLU=ON  NAKAYAMA, K?/AU,AUTH
L10              QUE  SPE=ON  ABB=ON  PLU=ON  UMEMURA, M?/AU,AUTH
L11              QUE  SPE=ON  ABB=ON  PLU=ON  OKAMOTO, M?/AU,AUTH
L12              QUE  SPE=ON  ABB=ON  PLU=ON  EISAI/CS,SO,PA OR ((NATIONAL
                  (1W)(INST OR INSTITUTE))(5A)(ADVANCED(1W)INDUSTRIAL)(5A)
                 (SCIENCE (3W)(TECH OR TECHNOL OR TECHNOLOGY)))/CS,SO,PA
L13              QUE  SPE=ON  ABB=ON  PLU=ON  ANTAGON? OR INHIBIT? OR PROH
                 IBIT? OR PREVENT? OR DIMINISH? OR REDUC? OR IMPED? OR DEP
                 RESS? OR SUPPRESS? OR REPRESS? OR OBSTRUCT? OR RESTRICT?
                 OR TERMINAT? OR BLOCK? OR STOP? OR RETARD? OR SLOW? OR DE
                 LAY? OR LIMIT? OR DECREAS? OR LOWER? OR LESSEN? OR MINIMI
                 Z? OR MINIMIS? OR DISRUPT?
L14              QUE  SPE=ON  ABB=ON  PLU=ON  FUNGUS OR FUNGI OR FUNGAL?
L15              QUE  SPE=ON  ABB=ON  PLU=ON  ANTIFUNG? OR FUNGICID? OR FU
                 NGISTAT?
L16              QUE  SPE=ON  ABB=ON  PLU=ON  SCREEN? OR TEST OR TESTING O
                 R TESTED OR EVALUAT? OR DETERMIN?
L19              QUE  SPE=ON  ABB=ON  PLU=ON  GWT1 OR (GWT(1W)(1 OR I)) OR
                  GWTI
L21              QUE  SPE=ON  ABB=ON  PLU=ON  SACCHAROMYC? OR CEREVIS?
L22              QUE  SPE=ON  ABB=ON  PLU=ON  TEST OR TESTING OR TESTED OR
                  DETECT? OR DETERMIN? OR ANALY? OR SENSE OR SENSED OR SEN
                 SING OR BIOSENS? OR ?ASSAY? OR ?MEASUR?
L24              QUE  SPE=ON  ABB=ON  PLU=ON  GPI
L25              QUE  SPE=ON  ABB=ON  PLU=ON  PI
L29              QUE  SPE=ON  ABB=ON  PLU=ON  (?PHOSPHATID? (1T)?INOSIT?)
                 OR (?PHOSPHATID? (1W)?INOSIT?)
L33              QUE  SPE=ON  ABB=ON  PLU=ON  CHROMATOG?
L34              QUE  SPE=ON  ABB=ON  PLU=ON  TLC
L127         21 SEA L19
L128        588 SEA (L21(10A)((L24 OR L25) OR L29))
L129      29842 SEA (L16 OR L22)(10A)((L13(5A) L14) OR L15)
L130         30 SEA (L127 OR L128) AND (L129 OR (L33 OR L34))
L131          4 SEA L130 AND (L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12)
L132         26 SEA L130 NOT L131
```

```
=> dup rem l63 l79 l97 l113 l126 l132
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PROCESSING COMPLETED FOR L113
PROCESSING COMPLETED FOR L126
PROCESSING COMPLETED FOR L132
L133         67 DUP REM L63 L79 L97 L113 L126 L132 (15 DUPLICATES REMOVED)
                ANSWERS '1-7' FROM FILE HCAPLUS
                ANSWERS '8-12' FROM FILE WPIX
                ANSWERS '13-17' FROM FILE MEDLINE
                ANSWERS '18-42' FROM FILE EMBASE
                ANSWERS '43-44' FROM FILE DRUGU
                ANSWERS '45-49' FROM FILE LIFESCI
                ANSWERS '50-51' FROM FILE BIOTECHDS
                ANSWERS '52-60' FROM FILE SCISEARCH
                ANSWERS '61-67' FROM FILE DISSABS
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=> fil hcap wpix medlin embase drugu lifesci biotechds scisearch dissabs
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L64             QUE  SPE=ON  ABB=ON  PLU=ON  AY<2003 OR PY<2003 OR PRY<20
                03 OR MY<2003 OR REVIEW/DT


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                ANSWERS '26-33' FROM FILE SCISEARCH
                ANSWERS '34-38' FROM FILE DISSABS

=> file stnguide
FILE 'STNGUIDE' ENTERED AT 13:26:30 ON 11 SEP 2009
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BIOTECHDS, SCISEARCH, DISSABS' - CONTINUE? (Y)/N:y



L135 ANSWER 1 OF 38  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2007:343893  HCAPLUS  Full-text
DOCUMENT NUMBER:          146:437636
TITLE:                    Biosynthesis and function of GPI
                          proteins in the yeast Saccharomyces
                          cerevisiae
AUTHOR(S):                Pittet, Martine; Conzelmann, Andreas
CORPORATE SOURCE:         Division of Biochemistry, Department of Medicine,
                          Fribourg, CH-1700, Switz.
SOURCE:                   Biochimica et Biophysica Acta, Molecular and Cell
                          Biology of Lipids (2007), 1771(3), 405-420
                          CODEN: BBMLFG; ISSN: 1388-1981
PUBLISHER:                Elsevier Ltd.
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
ED   Entered STN:  27 Mar 2007
AB    A review.  Like most other eukaryotes, Saccharomyces cerevisiae harbors a GPI
      anchoring machinery and uses it to attach proteins to membranes.  While a few
      GPI proteins reside permanently at the plasma membrane, a majority of them
      gets further processed and is integrated into the cell wall by a covalent
      attachment to cell wall glucans.  The GPI biosynthetic pathway is necessary
      for growth and survival of yeast cells.  The GPI lipids are synthesized in the
      ER and added onto proteins by a pathway comprising 12 steps, carried out by 23
      gene products, 19 of which are essential.  Some of the estimated 60 GPI
      proteins predicted from the genome sequence serve enzymic functions required
      for the biosynthesis and the continuous shape adaptations of the cell wall,
      others seem to be structural elements of the cell wall and yet others mediate
      cell adhesion.  Because of its genetic tractability S. cerevisiae is an
      attractive model organism not only for studying GPI biosynthesis in general,
      but equally for investigating the intracellular transport of GPI proteins and
      the peculiar role of GPI anchoring in the elaboration of fungal cell walls.
CC   10-0 (Microbial, Algal, and Fungal Biochemistry)
ST   review GPI protein synthesis endoplasmic reticulum
     Saccharomyces cell wall; Saccharomyces
     adaptation adhesion GPI protein transport review
IT   Endoplasmic reticulum
        (GPI synthesis in; biosynthesis and function of GPI
        proteins in yeast Saccharomyces cerevisiae)
IT   Adaptation, microbial
     Adhesion, biological
       Cell wall
       Saccharomyces cerevisiae
       Translation, genetic
         (biosynthesis and function of GPI proteins in yeast
         Saccharomyces cerevisiae)
IT   Biological transport
        (intracellular, GPI protein; biosynthesis and
        function of GPI proteins in yeast
        Saccharomyces cerevisiae)
IT   Glycophospholipids
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (phosphatidylinositol-containing; biosynthesis and function of
```

GPI proteins in yeast Saccharomyces cerevisiae)

OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)

REFERENCE COUNT: 167 THERE ARE 167 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L135 ANSWER 2 OF 38 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:10721 HCAPLUS Full-text

DOCUMENT NUMBER: 136:79717

TITLE: Screen for identifying inhibitors of GPI anchoring

INVENTOR(S): Bulawa, Christine; Keaveney, Marie; Blackman, Ronald K.

PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000919	A2	20020103	WO 2001-US20149	20010622 <--
WO 2002000919	A3	20030206		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 20020072051	A1	20020613	US 2001-887489	20010622 <--
PRIORITY APPLN. INFO.:			US 2000-213623P P	20000623 <--

ED Entered STN: 04 Jan 2002

AB Methods for identifying compds. that are capable of activating the UPR (unfolded protein response) pathway, inhibition of glycosylphosphatidylinositol (GPI) anchoring, and/or antifungal activity are disclosed. Also disclosed are methods for treating fungal infections in an organism using compds. identified as having antifungal activity, and methods for treating a protozoan infection in an organism using compds. identified as inhibiting GPI anchoring.

IC ICM C12Q001-00

CC 1-1 (Pharmacology)
Section cross-reference(s): 10

ST glycosylphosphatidylinositol anchoring inhibitor antifungal drug screening

IT Ameba
(amebiasis; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to reporter gene in yeast cell)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(assay, secondary screen; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides)

IT Pleura, disease
(fungal infection; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to reporter gene in yeast cell)

IT Tinea (skin disease)
(fungal; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to reporter gene in yeast cell)

IT Infection
Intestine, disease
(giardiasis; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to reporter gene in yeast cell)

IT Fungicide resistance
(in secondary screen; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides)

IT Lung, disease
(infection, fungal, hypersensitivity; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to reporter gene in yeast cell)

IT Urogenital system, disease
(infection, fungal; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to reporter gene in yeast cell)

IT Babesia
Cryptosporidium
(infection; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to reporter gene in yeast cell)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(labeling of, secondary screen; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(lacZ; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to

reporter gene in yeast cell)
IT Infection
(leishmaniasis; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to reporter gene in yeast cell)
IT Protozoacides
(leishmanicides; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to reporter gene in yeast cell)
IT Glycolipoproteins
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(phosphatidylinositol-containing, maturation, in secondary screen; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides)
IT Glycophospholipids
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(phosphatidylinositol-containing; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to reporter gene in yeast cell)
IT Infection
(pulmonary, fungal, hypersensitivity; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to reporter gene in yeast cell)
IT Amebicides
Antimalarials
Drug screening
Fungicides
Genetic vectors
High throughput screening
Malaria
Mycosis
Protozoacides
Saccharomyces
Saccharomyces cerevisiae
Yeast
(screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to reporter gene in yeast cell)
IT Genetic element
Proteins
Reporter gene
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to

reporter gene in yeast cell)
IT Infection
(urogenital, fungal; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to reporter gene in yeast cell)
IT 9014-00-0, Luciferase 9031-11-2, β-Galactosidase
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene encoding; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to reporter gene in yeast cell)
IT 51059-75-7 100217-01-4
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(lipid labeling by, secondary screen; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides)
IT 385846-79-7
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(nucleotide sequence; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to reporter gene in yeast cell)
IT 87-89-8, Inositol
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(protein incorporation, secondary screen; screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides)
IT 385612-19-1
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(screen inhibitors of GPI anchoring and activators of unfolded protein response as fungicides and protozoacides by expressing vector comprising unfolded protein response element linked to reporter gene in yeast cell)
IT 385851-15-0
RL: PRP (Properties)
(unclaimed sequence; screen for identifying inhibitors of GPI anchoring)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ifull 3-4
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, WPIX, EMBASE, DRUGU, LIFESCI, BIOTECHDS, SCISEARCH, DISSABS' - CONTINUE? (Y)/N:y

L135 ANSWER 3 OF 38 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 1997-245104 [22] WPIX
DOC. NO. CPI: C1997-079452 [22]
TITLE: Human mevalonate pyrophosphate decarboxylase coding sequence - used for screening for MPD inhibitors, which regulate and control cholesterol synthesis
DERWENT CLASS: B04; D16
INVENTOR: HUWYLER L R; TOTH M J
PATENT ASSIGNEE: (CIBA-C) CIBA GEIGY AG; (NOVS-C) NOVARTIS AG; (NOVS-C) NOVARTIS FINANCE CORP
COUNTRY COUNT: 63

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC	
WO 9714787	A1	19970424	(199722)*	EN	37[0]		<--
AU 9672894	A	19970507	(199735)	EN			<--
US 5837839	A	19981117	(199902)	EN			<--

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9714787	A1	WO 1996-EP4394	19961010
US 5837839	A Provisional	US 1995-5652P	19951018
AU 9672894	A	AU 1996-72894	19961010
US 5837839	A	US 1996-733825	19961018

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9672894	A	Based on	WO 9714787 A

PRIORITY APPLN. INFO: US 1995-5652P 19951018
US 1996-733825 19961018
INT. PATENT CLASSIF.:
IPC RECLASSIF.: C12N0015-60 [I,A]; C12N0015-60 [I,C]; C12N0009-88 [I,A]; C12N0009-88 [I,C]
ECLA: C12N0009-88
ICO: M12N0207:00
USCLASS NCLM: 536/023.200
NCLS: 435/007.720; 435/069.100; 435/232.000; 435/252.300; 435/320.100

BASIC ABSTRACT:

WO 1997014787 A1 UPAB: 20050517

A nucleotide sequence (I) that codes for human mevalonate pyrophosphate decarboxylase (MPD) comprising a sequence which when expressed in a host cell results in the production of active MPD, is new.

USE - (I) can be used for producing large quantities of purified MPD. The MPD can be used in assays to screen for inhibitors of MPD which can potentially be used as therapeutics to regulate and control cholesterol synthesis and cell proliferation. (I) can also be used to produce MPD, which is used to generate antisera which can be used to aid in the diagnosis of patients suffering from metabolic diseases that affect the cholesterol synthetic pathway. Inhibitors of MPD could also be used in treating lymphomas and phenylketonuria. MPD could be used as molecular weight markers, or as a dietary food supplement of proteins. MPD could also be used as a starting

material in the chemical synthesis of polyisoprene-containing compounds that include taxol.

DOCUMENTATION ABSTRACT:

WO9714787

A nucleotide sequence (I) that codes for human mevalonate pyrophosphate decarboxylase (MPD) comprising a sequence which when expressed in a host cell results in the production of active MPD, is new.

Also claimed is an assay for measuring the ability of a compound to regulate the activity of MPD comprising:

(a) measuring the MPD activity of a protein recombinantly produced by the expression of (I) in the presence of a candidate compound; and

(b) comparing the MPD activity in the presence of the candidate compound to MPD activity of the protein.

USE

(I) can be used for producing large quantities of purified MPD. The MPD can be used in assays to screen for inhibitors of MPD which can potentially be used as therapeutics to regulate and control cholesterol synthesis and cell proliferation. (I) can also be used to produce MPD, which is used to generate antisera which can be used to aid in the diagnosis of patients suffering from metabolic diseases that affect the cholesterol synthetic pathway.

Inhibitors of MPD could also be used in treating lymphomas and phenylketonuria. MPD could be used as molecular weight markers, or as a dietary food supplement of proteins. MPD could also be used as a starting material in the chemical synthesis of polyisoprene-containing compounds that include taxol.

MORE SPECIFICALLY

The specification includes the DNA sequence (1800 bp) and amino acid sequence (400 residues) of human liver MPD.

EXAMPLE

Livers from 6 freshly sacrificed rats were collected on ice, rinsed in homogenisation buffer, diced and homogenised with 300 ml of the buffer containing 0.1 mM leupeptin, 0.75 mg/l aprotinin, and 0.1 mM phenylmethanesulphonyl fluoride. The active fraction was purified, and subjected to trypsin digestion. The resulting peptides were isolated and sequenced, before being used to design PCR primers.

The primers were used to isolate a cDNA fragment from a rat liver cDNA library. Three identical clones were isolated and sequenced. Analysis suggested that only half of the open reading frame was encoded. This partial cDNA clone was used to probe a human liver cDNA library, and identified the 1800 bp sequence given in the specification.

(GS4)

PREFERRED SEQUENCES

The MPD activity can be measured by similarity of amino acid sequence, Michaelis-Menton constants (Km), weight of the holoenzyme, terminal nucleotide sequence, pI, inhibition constants (Ki) of various inhibitors, or by enzymatic activity. The MPD activity of the protein encoded by (I) is preferably enzymatic activity as measured by the coupled spectrometric assay or as the conversion of labelled mevalonate pyrophosphate into isopentenyl.

PREFERRED ASSAY

In the assay, the MPD activity is preferably measured by the conversion of labelled mevalonate pyrophosphate into isopentenyl or is measured by the coupled spectrophotometric assay.

FILE SEGMENT: CPI

MANUAL CODE: CPI: B04-E02E; B04-E03E; B04-L0600E; B11-C08E3; B12-K04E; D05-H09; D05-H12A; D05-H17A3

L135 ANSWER 4 OF 38 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 1991-016644 [03] WPIX
DOC. NO. CPI: C1991-007163 [21]
TITLE: New protein with high urate oxidase activity - and recombinant DNA encoding it, vectors and transformed cells, used for treating hyperuricaemia, etc.
DERWENT CLASS: B04; D16
INVENTOR: CAPUT D; FERRARA P; GUILLEMOT J; GUILLEMOT J C; KAGHAD M; LABRE E; LARBRE E; LAURENT P; LEGOUX R; LEPLATOIS P; LOISON G; LUPKER J; SALOME M; SALOME M L V
PATENT ASSIGNEE: (SNFI-C) ELF SANOFI; (SNFI-C) SANOFI SA
COUNTRY COUNT: 38

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC	
EP 408461	A	19910116	(199103)*	EN	68[14]		<--
WO 9100909	A	19910124	(199107)	EN			<--
FR 2649720	A	19910118	(199110)	FR			<--
PT 94680	A	19910418	(199118)	PT			<--
AU 9060523	A	19910206	(199119)	EN			<--
ZA 9005516	A	19910424	(199122)	EN			<--
FI 9101212	A	19910312	(199123)	FI			<--
NO 9100982	A	19910510	(199131)	NO			<--
BR 9006855	A	19910806	(199136)	PT			<--
FR 2656530	A	19910705	(199137)	FR			<--
FR 2657785	A	19910809	(199144)	FR			<--
HU 56884	T	19911028	(199147)	HU			<--
JP 04501807	W	19920402	(199220)	JA	41		<--
NZ 234453	A	19930127	(199310)	EN			<--
AU 636637	B	19930506	(199325)	EN			<--
US 5382518	A	19950117	(199509)	EN	58[4]		<--
US 5541098	A	19960730	(199636)	EN	55[14]		<--
EP 408461	B1	19961016	(199646)	FR	82[14]		<--
DE 69028884	E	19961121	(199701)	DE			<--
ES 2095243	T3	19970216	(199714)	ES			<--
IL 95057	A	19970713	(199734)	EN			<--
JP 2664804	B2	19971022	(199747)	JA	52[0]		<--
IE 77158	B	19971203	(199803)	EN			<--
BR 1100404	A3	19980422	(199822)	PT			<--
BR 1100689	A3	19980428	(199823)	PT			<--
RU 2105812	C1	19980227	(199841)	RU			<--
HU 215948	B	19990329	(199921)	HU			<--
CA 2035900	C	20000111	(200023)	FR			<--
KR 159107	B1	19981116	(200030)	KO			<--
FI 105047	B1	20000531	(200033)	FI			<--
NO 308139	B1	20000731	(200044)	NO			<--

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 408461 A		EP 1990-402023	19900713
FR 2649720 A		FR 1989-9550	19890713
FR 2656530 A		FR 1989-9550	19890713
FR 2657785 A		FR 1989-9550	19890713

FR 2649720 A	FR 1989-909550 19890713
FR 2649720 A	FR 1989-17466 19891229
FR 2656530 A	FR 1989-17466 19891229
FR 2657785 A	FR 1989-17466 19891229
FR 2656530 A	FR 1989-617466 19891229
FR 2649720 A	FR 1990-1368 19900206
FR 2656530 A	FR 1990-1368 19900206
FR 2657785 A	FR 1990-1368 19900206
NZ 234453 A	NZ 1990-234453 19900711
IL 95057 A	IL 1990-95057 19900712
AU 636637 B	AU 1990-60523 19900713
CA 2035900 C	CA 1990-2035900 19900713
DE 69028884 E	DE 1990-69028884 19900713
EP 408461 B1	EP 1990-402023 19900713
DE 69028884 E	EP 1990-402023 19900713
ES 2095243 T3	EP 1990-402023 19900713
HU 215948 B	HU 1990-6046 19900713
IE 77158 B	IE 1990-2559 19900713
JP 04501807 W	JP 1990-510514 19900713
JP 2664804 B2	JP 1990-510514 19900713
US 5382518 A	WO 1990-FR532 19900713
US 5541098 A Cont of	WO 1990-FR532 19900713
JP 2664804 B2	WO 1990-FR532 19900713
RU 2105812 C1	WO 1990-FR532 19900713
HU 215948 B	WO 1990-FR532 19900713
CA 2035900 C	WO 1990-FR532 19900713
FI 105047 B1	WO 1990-FR532 19900713
NO 308139 B1	WO 1990-FR532 19900713
ZA 9005516 A	ZA 1990-5516 19900713
FI 105047 B1	FI 1991-1212 19910312
NO 308139 B1	NO 1991-982 19910312
RU 2105812 C1	SU 1991-4895030 19910312
KR 159107 B1	KR 1991-700276 19910313
US 5382518 A Cont of	US 1991-659408 19910425
US 5541098 A Cont of	US 1991-659408 19910425
US 5382518 A	US 1992-920519 19920728
US 5541098 A Div Ex	US 1992-920519 19920728
US 5541098 A	US 1994-314586 19940928
BR 1100404 A3	BR 1997-1100404 19970502
BR 1100689 A3	BR 1997-1100689 19970508

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 636637 B	Previous Publ	AU 9060523 A
DE 69028884 E	Based on	EP 408461 A
ES 2095243 T3	Based on	EP 408461 A
FI 105047 B1	Previous Publ	FI 9101212 A
HU 215948 B	Previous Publ	HU 56884 T
JP 2664804 B2	Previous Publ	JP 04501807 W
NO 308139 B1	Previous Publ	NO 9100982 A
US 5541098 A	Div ex	US 5382518 A
JP 04501807 W	Based on	WO 9100909 A
AU 636637 B	Based on	WO 9100909 A
US 5382518 A	Based on	WO 9100909 A
JP 2664804 B2	Based on	WO 9100909 A
HU 215948 B	Based on	WO 9100909 A
CA 2035900 C	Based on	WO 9100909 A

PRIORITY APPLN. INFO: FR 1990-1368 19900206
FR 1989-9550 19890713
FR 1989-17466 19891229
FR 1989-909550 19890713
FR 1989-617466 19891229

INT. PATENT CLASSIF.:
MAIN: C12N015-53
SECONDARY: C12N001-00
IPC RECLASSIF.: A61K0038-43 [I,C]; A61K0038-43 [I,C]; A61K0038-44 [I,A]; A61K0038-44 [I,A]; C07K [I,S]; C07K0014-00 [I,A]; C07K0014-00 [I,C]; C07K0014-37 [I,A]; C07K0014-37 [I,C]; C07K0014-37 [I,C]; C07K0014-38 [I,A]; C07K0014-395 [I,A]; C07K0014-41 [I,A]; C07K0014-41 [I,C]; C12N0001-19 [I,A]; C12N0001-19 [I,C]; C12N0001-21 [I,A]; C12N0001-21 [I,C]; C12N0015-09 [I,A]; C12N0015-09 [I,C]; C12N0015-53 [I,A]; C12N0015-53 [I,C]; C12N0015-63 [I,A]; C12N0015-63 [I,C]; C12N0015-70 [I,A]; C12N0015-70 [I,C]; C12N0015-81 [I,A]; C12N0015-81 [I,C]; C12N0015-85 [I,A]; C12N0015-85 [I,C]; C12N0005-10 [I,A]; C12N0005-10 [I,A]; C12N0005-10 [I,C]; C12N0005-10 [I,C]; C12N0005-16 [I,A]; C12N0005-16 [I,C]; C12N0009-02 [I,A]; C12N0009-02 [I,C]; C12N0009-06 [I,A]; C12N0009-06 [I,C]; C12P0021-00 [I,A]; C12P0021-00 [I,C]; C12R0001-67 [N,A]; C12R0001-865 [N,A]
ECLA: C12N0009-06F2
ICO: M12N0207:00
BASIC ABSTRACT:

EP 408461 A UPAB: 20050820

The protein of formula (I), opt. preceeded by Met, with specific urate oxidase activity at least 16 (especially about 30) u/mg is new. Also included are proteins substantially homologous with (I). Also new are (I) recombinant genes including a DNA sequence (reproduced in the specification) encoding (I); (2) expression vectors containing such genes and (3) procaryotic or eucaryotic cells transformed with these vectors.

USE/ADVANTAGE - Urate oxidase (uricase) is useful for treatment of hyperuricaemia and kidney stones, and as an adjuvant in chemotherapy with cytolytic agnents. It can now be produced in recombinant avoiding the problems (difficult purification, possible contamination by aflatoxins and low specific activity) associated with culture of Aspergillus flavus. Materials (I) has mol. weight 33.5 kD (by 2-dimensional gel electrophoresis) and isoelectric point about 8, representing at least 90% of the weight of protein. Purity, by liquid chromatography in C8-silica is over 80% and (I) may have a blocking gp. at N-terminal Ser. For expression of the gene in animal cells, the non-translated sequence AGCTTGCCGCCACT is situated immediately ahead of the functional gene. Where Saccharomyces cerevisiae is used, a strain having a mutation in at least one gene responsible for Leu or uracil synthesis is chosen.

FILE SEGMENT: CPI
MANUAL CODE: CPI: B04-B02C2; B04-B04A; B12-A07; B12-G03; D05-C03B; D05-H03B; D05-H04; D05-H05; D05-H11; D05-H12

=> d bib ed ab ind 5-38
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, WPIX, EMBASE, DRUGU, LIFESCI, BIOTECHDS, SCISEARCH, DISSABS' - CONTINUE? (Y)/N:y

L135 ANSWER 5 OF 38 EMBASE

AN 2002354334 EMBASE Full-text
TI Novel strategies in antifungal lead discovery.
AU Jiang, Bo (correspondence); Roemer, Terry
CS Elitra Canada, 225 President Kennedy West, Montreal, Que. H2X 3Y8, Canada. troemer@elitra.com; bjiang@elitra.com
AU Bussey, Howard
CS Department of Biology, McGill University, Stewart Biology Building, 1205 Dr Penfield Avenue, Montreal, Que. H3A 1B1, Canada. hbusse@po-box.mcgill.ca
SO Current Opinion in Microbiology, (Oct 2002) Vol. 5, No. 5, pp. 466-471.
Refs: 37
ISSN: 1369-5274 CODEN: COMIF7
CY United Kingdom
DT Journal; General Review; (Review)
FS 037 Drug Literature Index
038 Adverse Reactions Titles
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 24 Oct 2002
Last Updated on STN: 24 Oct 2002
ED Entered STN: 24 Oct 2002
Last Updated on STN: 24 Oct 2002
AB There have been significant developments in fungal genomics over the past year. The recently released genome sequences of Aspergillus fumigatus and Cryptococcus neoformans have provided unprecedented opportunities for comparative genomics studies of many clinically relevant fungal pathogens. Emerging experimental analysis tools, such as fitness profiling and protein microarrays, have greatly enhanced our ability to conduct genome-wide functional studies.
CT Medical Descriptors:
allele
amino acid sequence
*Aspergillus fumigatus
assay
bioinformatics
Candida albicans
*Cryptococcus neoformans
DNA sequence
drug resistance
gene
gene deletion
gene disruption
gene sequence
*genome
human
mutagenesis
mycosis: DT, drug therapy
nonhuman
nucleotide sequence
phenotype
polyacrylamide gel electrophoresis
polymerase chain reaction
proteomics
review
Saccharomyces cerevisiae
toxicity: SI, side effect
virulence
CT Drug Descriptors:
amphotericin B: AE, adverse drug reaction

amphotericin B: DT, drug therapy
*antifungal agent
calmodulin
caspofungin
DNA
ergosterol
fk 506 binding protein: EC, endogenous compound
fluconazole: DT, drug therapy
fosfomycin
galactose
gene product
glyoxylic acid
hybrid protein
isocitrate lyase
itraconazole: DT, drug therapy
malate synthase
mycophenolic acid
nucleotide: EC, endogenous compound
nystatin
oxidoreductase
phosphatidylinositide
polyene: AE, adverse drug reaction
polyene: DT, drug therapy
proteasome inhibitor
protein
rapamycin
sorbitol
synthetase
tacrolimus
tricarboxylic acid

RN (amphotericin B) 1397-89-3, 30652-87-0; (caspofungin) 189768-38-5; (DNA) 9007-49-2; (ergosterol) 23637-22-1, 2418-45-3, 3992-98-1, 57-87-4; (fluconazole) 86386-73-4; (fosfomycin) 23155-02-4; (galactose) 26566-61-0, 50855-33-9, 59-23-4; (glyoxylic acid) 298-12-4; (isocitrate lyase) 9045-78-7; (itraconazole) 84625-61-6; (malate synthase) 9013-48-3; (mycophenolic acid) 23047-11-2, 24280-93-1; (nystatin) 1400-61-9, 34786-70-4, 62997-67-5; (oxidoreductase) 9035-73-8, 9035-82-9, 9037-80-3, 9055-15-6; (protein) 67254-75-5; (rapamycin) 53123-88-9; (sorbitol) 26566-34-7, 50-70-4, 53469-19-5; (synthetase) 9031-56-5, 9031-57-6; (tacrolimus) 104987-11-3

CN caspofungin; fk 506

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AN 2002451541 EMBASE Full-text

TI Rapamycin insensitivity in Schistosoma mansoni is not due to FKBP12 functionality.

AU Rossi, Alessandro; Klinkert, Mo-Quen (correspondence)

CS Department of Parasitology, Institute for Tropical Medicine, University of Tubingen, Wilhelmstrasse 27, 72074 Tubingen, Germany. mo.klinkert@uni-tueb ingen.de

AU Pica-Mattoccia, Livia; Cioli, Donato

CS Institute for Cell Biology, Consiglio Nazionale delle Ricerche, Rome, Italy.

SO Molecular and Biochemical Parasitology, (Nov 2002) Vol. 125, No. 1-2, pp. 1-9.
Refs: 31
ISSN: 0166-6851 CODEN: MBIPDP

PUI S 0166-6851(02)00207-4

CY Netherlands

DT Journal; Article
FS 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 3 Jan 2003
Last Updated on STN: 3 Jan 2003
ED Entered STN: 3 Jan 2003
Last Updated on STN: 3 Jan 2003
AB Rapamycin (RAPA) is a well-known immunosuppressant, the action of which is mediated by the immunophilin FKBP12. Upon RAPA binding, FKBP12 forms ternary complexes with phosphatidyl inositol related kinases known as the target of RAPA (TOR), which can lead to a mitotic block at the G1-S phase transition. Such an antiproliferative effect makes RAPA an attractive anticancer, antifungal or antiparasitic compound. In this study, we found the helminth parasite Schistosoma mansoni to be insensitive to the drug. In order to elucidate the mechanism underlying RAPA resistance, the S. mansoni drug receptor FKBP12 (SmFKBP12) was cloned for functional analysis. Western blot experiments showed that the protein is constitutively expressed in all life cycle stages and in both male and female parasites. The Escherichia coli-synthesised recombinant protein possessed enzymatic activity, which was inhibitable by RAPA. Moreover, SmFKBP12 was able to complement mutant Saccharomyces cerevisiae cells lacking FKBP12 in their RAPA sensitivity phenotype, leading us to conclude that SmFKBP12 is expressed in yeast in a functional form and capable of interacting with the drug and yeast TOR kinase. Even though the wild type SmFKBP12 appeared to restore a large part of RAPA sensitivity, a mutation of Asp(89)-Lys(90) to Pro(89)-Gly(90) in the schistosome protein was found to be more effective and restored drug sensitivity to the same level as the endogenous yeast protein. Despite ternary complex formation, our results suggest that additional unknown factors other than a functional drug receptor are implicated in drug resistance mechanisms.
CT Medical Descriptors:
amino acid sequence
article
controlled study
enzyme activity
Escherichia coli
life cycle
molecular cloning
mutation
nonhuman
*nucleotide sequence
open reading frame
phenotype
priority journal
protein expression
protein interaction
Saccharomyces cerevisiae
*Schistosoma mansoni
sequence alignment
sequence analysis
Western blotting
CT Drug Descriptors:
*drug receptor
*rapamycin
*receptor FKBP12
unclassified drug
RN (rapamycin) 53123-88-9
GEN GENBANK AY118110 submitted number; GENBANK R95612 referred number; P20081 referred number

L135 ANSWER 7 OF 38 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
AN 2003458043 EMBASE Full-text
TI The Effect of the erg26-1 Mutation on the Regulation of Lipid Metabolism in Saccharomyces cerevisiae.
AU Baudry, Karen; Swain, Evelyn; Germann, Melody; Nickels Jr., Joseph T. (correspondence)
CS Department of Biochemistry, MCP Hahnemann University, Philadelphia, PA 19129, United States. Joseph.Nickels@drexel.edu
AU Henry, Karl; Edlind, Thomas
CS Dept. of Microbiology and Immunology, MCP Hahnemann University, Philadelphia, PA 19129, United States.
AU Rahier, Alain; Rondet, Sabine
CS Dept. d'Enzymologie Cell. et Molec., Institut de Botanique, Strasbourg Cedex, France.
AU Batta, Ashok; Tint, G. Stephen
CS Department of Veteran Affairs, New Jersey Medical School, East Orange, NJ 07018, United States.
AU Mandala, Suzanne; Kurtz, Myra
CS Department of Biochemistry, Merck Research Laboratories, Rahway, NJ 07065, United States.
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SO Journal of Biological Chemistry, (20 Apr 2001) Vol. 276, No. 16, pp. 12702-12711.
Refs: 61
ISSN: 0021-9258 CODEN: JBCHA3
CY United States
DT Journal; Article
FS 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 4 Dec 2003
Last Updated on STN: 4 Dec 2003
ED Entered STN: 4 Dec 2003
Last Updated on STN: 4 Dec 2003
AB A temperature-sensitive Saccharomyces cerevisiae mutant harboring a lesion in the ERG26 gene has been isolated. ERG26 encodes 4α-carboxysterol-C3 dehydrogenase, one of three enzymatic activities required for the conversion of 4,4-dimethylzymosterol to zymosterol. Gas chromatography/mass spectrometry analyses of sterols in this mutant, designated erg26-1, revealed the aberrant accumulation of a 4-methyl-4-carboxy zymosterol intermediate, as well as a novel 4-carboxysterol. Neutral lipid radiolabeling studies showed that erg26-1 cells also harbored defects in the rate of biosynthesis and steady-state levels of mono-, di-, and triglycerides. Phospholipid radiolabeling studies showed defects in the rate of biosynthesis of both phosphatidic acid and phosphatidylinositol. Biochemical studies revealed that microsomes isolated from erg26-1 cells contained greatly reduced 4α-carboxysterol-C3 dehydrogenase activity when compared with microsomes from wild type cells. Previous studies have shown that loss of function mutations in either of the fatty acid elongase genes SUR4/ELO3 or FEN1/GNS1/ELO2 can "by-pass" the essentiality of certain ERG genes (Ladeveze, V., Marcireau, C., Delourme, D., and Karst, F. (1993) Lipids 28, 907-912; Silve, S., Leplatois, P., Josse, A., Dupuy, P. H., Lanau, C., Kaghad, M., Dhers, C., Picard, C., Rahier, A., Taton, M., Le Fur, G., Caput, D., Ferrara, P., and Loison, G. (1996) Mol. Cell. Biol. 16, 2719-

2727). Studies presented here have shown that this sphingolipid-dependent "bypass" mechanism did not suppress the essential requirement for zymosterol biosynthesis. However, studies aimed at understanding the underlying physiology behind the temperature-sensitive growth defect of erg26-1 cells showed that the addition of several antifungal compounds to the growth media of erg26-1 cells could suppress the temperature-sensitive growth defect. Fluorescence microscopic analysis showed that GFP-Erg26p and GFP-Erg27p fusion proteins were localized to the endoplasmic reticulum. Two-hybrid analysis indicated that Erg25p, Erg26p, and Erg27p, which are required for the biosynthesis of zymosterol, form a complex within the cell.

CT Medical Descriptors:
article
biosynthesis
controlled study
  elo2 gene
  elo3 gene
endoplasmic reticulum
enzyme activity
  *erg26 1 gene
  fen1 gene
fluorescence microscopy
  fungal cell
  *fungal gene
  fungus growth
  gas chromatography
  gene isolation
  *gene mutation
genetic code
  gns1 gene
  growth inhibition
isotope labeling
*lipid metabolism
lipogenesis
mass spectrometry
nonhuman
priority journal
  protein localization
  *Saccharomyces cerevisiae
steady state
  sur4 gene
temperature sensitivity
two hybrid system
wild type

CT Drug Descriptors:
4,4 dimethylzymosterol: EC, endogenous compound
4alpha carboxysterol c3 dehydrogenase: EC, endogenous compound
  antifungal agent
diacylglycerol: EC, endogenous compound
  green fluorescent protein erg26p fusion protein
  green fluorescent protein erg27p fusion protein
  hybrid protein
*lipid: EC, endogenous compound
monoacylglycerol: EC, endogenous compound
oxidoreductase: EC, endogenous compound
  phosphatidic acid: EC, endogenous compound
  phosphatidylinositol: EC, endogenous compound
phospholipid
sphingolipid: EC, endogenous compound
triacylglycerol: EC, endogenous compound
unclassified drug

zymosterol: EC, endogenous compound
RN (4,4 dimethylzymosterol) 7448-02-4; (lipid) 66455-18-3; (oxidoreductase) 9035-73-8, 9035-82-9, 9037-80-3, 9055-15-6; (zymosterol) 128-33-6

L135 ANSWER 8 OF 38 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
AN 2001422809 EMBASE Full-text
TI Lag1p and Lac1p are essential for the Acyl-CoA-dependent ceramide synthase reaction in Saccharomyces cerevisiae.
AU Schorling, S.; Vallee, B.; Barz, W.P.; Riezman, H. (correspondence); Oesterhelt, D.
CS Biozentrum of the Univ. of Basel, CH-4056 Basel, Switzerland. Howard.Riezman@unibas.ch
SO Molecular Biology of the Cell, (2001) Vol. 12, No. 11, pp. 3417-3427.
Refs: 38
ISSN: 1059-1524 CODEN: MBCEEV
CY United States
DT Journal; Article
FS 029 Clinical and Experimental Biochemistry
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 20 Dec 2001
Last Updated on STN: 20 Dec 2001
ED Entered STN: 20 Dec 2001
Last Updated on STN: 20 Dec 2001
AB Lag1p and Lac1p are two homologous transmembrane proteins of the endoplasmic reticulum in Saccharomyces cerevisiae. Homologous genes have been found in a wide variety of eukaryotes. In yeast, both genes, LAC1 and LAG1, are required for efficient endoplasmic reticulum-to-Golgi transport of glycosylphosphatidylinositol-anchored proteins . In this study, we show that lag1Δlac1Δ cells have reduced sphingolipid levels due to a block of the fumonisin B1-sensitive and acyl-CoA-dependent ceramide synthase reaction. The sphingolipid synthesis defect in lag1Δlac1Δ cells can be partially corrected by overexpression of YPC1 or YDC1, encoding ceramidases that have been reported to have acyl-CoA-independent ceramide synthesis activity. Quadruple mutant cells (lag1Δlac1Δypc1Δydc1Δ) do not make any sphingolipids, but are still viable probably because they produce novel lipids. Moreover, lag1Δlac1Δ cells are resistant to aureobasidin A, an inhibitor of the inositolphosphorylceramide synthase, suggesting that aureobasidin A may be toxic because it leads to increased ceramide levels. Based on these data, LAG1 and LAC1 are the first genes to be identified that are required for the fumonisin B1-sensitive and acyl-CoA-dependent ceramide synthase reaction.
CT Medical Descriptors:
animal cell
apoptosis
article
*endoplasmic reticulum
enzyme activity
*enzyme mechanism
gene deletion
Golgi complex
lipid metabolism
nonhuman
priority journal
protein expression
protein transport
reaction analysis
Saccharomyces cerevisiae

signal transduction
CT Drug Descriptors:
*acyl coenzyme A
aureobasidin A
fumonisin B1
glycosylphosphatidylinositol
membrane protein
*sphingosine acyltransferase
RN (aureobasidin A) 127785-64-2; (fumonisin B1) 116355-83-0; (sphingosine acyltransferase) 37257-09-3

L135 ANSWER 9 OF 38 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
AN 2002008757 EMBASE Full-text
TI The yeast cell-wall salvage pathway.
AU Popolo, L. (correspondence); Gualtieri, T.; Ragni, E.
CS Universita degli Studi di Milano, Dipto. di Fisiol. e Biochim. Gen., Via Celoria 26, 20133 Milano, Italy. Laura.Popolo@unimi.it
SO Medical Mycology, Supplement, (2001) Vol. 39, No. 1, pp. 111-121.
Refs: 53
ISSN: 0966-8454 CODEN: MMSUFX
CY United Kingdom
DT Journal; General Review; (Review)
FS 037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 17 Jan 2002
Last Updated on STN: 17 Jan 2002
ED Entered STN: 17 Jan 2002
Last Updated on STN: 17 Jan 2002
AB The integrity of the cell wall depends on the synthesis and correct assembly of its individual components. Several environmental factors, such as temperature up-shift, treatments with mating factors or with specific cell wall-perturbing drugs, or genetic factors, such as inactivation of cell wall-related genes (for example FKS1 or GAS1) can impair construction of the cell wall. As the cell wall is essential for preserving the osmotic integrity of the cell, several responses are triggered in response to cell- wall damage. This review focuses on the activation of salvage pathways that guarantee cell survival through remodeling of the extracellular matrix. These researches have useful implication for the study of similar pathways in human fungal pathogens, and for the evaluation of the efficacy of new antifungal drugs.
CT Medical Descriptors:
Aspergillus fumigatus
biogenesis
Candida albicans
cell survival
*cell wall
DNA microarray
drug efficacy
environmental factor
experimentation
extracellular matrix
fungal genetics
fungus mutant
fungus mutation
gene deletion
human
nonhuman
osmosis

protein phosphorylation
review
Saccharomyces cerevisiae
signal transduction
stress
temperature
*yeast
CT Drug Descriptors:
1,3 beta glucanase
*antifungal agent: DV, drug development
beta 1,3 glucan: EC, endogenous compound
beta 1,6 glucan: EC, endogenous compound
calcineurin: EC, endogenous compound
calcofluor
cell membrane protein: EC, endogenous compound
chitin: EC, endogenous compound
cyclosporin A: DV, drug development
dodecyl sulfate sodium
fks1 protein: EC, endogenous compound
fungal protein: EC, endogenous compound
gas1 protein: EC, endogenous compound
glucan: EC, endogenous compound
glycosylphosphatidylinositol: EC, endogenous compound
immunosuppressive agent: DV, drug development
mannoprotein: EC, endogenous compound
mitogen activated protein kinase: EC, endogenous compound
nikkomycin Z: DV, drug development
protein kinase C: EC, endogenous compound
protein kinase C 1: EC, endogenous compound
sorbitol
tacrolimus: DV, drug development
unclassified drug
vanadic acid: DV, drug development
zymolyase 100 T
RN (1,3 beta glucanase) 9073-49-8; (beta 1,3 glucan) 9051-97-2; (calcineurin) 137951-12-3; (calcofluor) 4404-43-7; (chitin) 1398-61-4; (cyclosporin A) 59865-13-3, 63798-73-2; (dodecyl sulfate sodium) 151-21-3; (glucan) 9012-72-0, 9037-91-6; (mitogen activated protein kinase) 142243-02-5; (nikkomycin Z) 59456-70-1; (protein kinase C) 141436-78-4; (sorbitol) 26566-34-7, 50-70-4, 53469-19-5; (tacrolimus) 104987-11-3; (vanadic acid) 12260-63-8, 13981-20-9, 37353-31-4
CN fk 506; zymolyase 100 T

L135 ANSWER 10 OF 38 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
AN 2002008747 EMBASE Full-text
TI Molecular organization of the cell wall of Candida albicans.
AU Klis, F.M. (correspondence); De Groot, P.; Hellingwerf, K.
CS Swammerdam Inst. for Life Sciences, University of Amsterdam, Nieuwe Achtergracht 166, 1018 WV Amsterdam, Netherlands. klis@science.uva.nl
SO Medical Mycology, Supplement, (2001) Vol. 39, No. 1, pp. 1-8.
Refs: 76
ISSN: 0966-8454 CODEN: MMSUFX
CY United Kingdom
DT Journal; General Review; (Review)
FS 037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English

ED Entered STN: 17 Jan 2002
Last Updated on STN: 17 Jan 2002
ED Entered STN: 17 Jan 2002
Last Updated on STN: 17 Jan 2002
AB We have recently presented a molecular model of the cell wall of Saccharomyces cerevisiae. Here we discuss the evidence that a similar model is also valid for Candida albicans. We further discuss how cell-wall proteins are linked to the skeletal layer of the wall, and their potential functions. We emphasize that the composition and structure of the cell wall depends on growth conditions. Finally, cell-wall damage seems to activate a salvage mechanism resulting in restructuring of the cell wall.
CT Medical Descriptors:
*Candida albicans
carbohydrate synthesis
cell damage
cell structure
*cell wall
fungus growth
fungus hyphae
molecular model
nonhuman
review
Saccharomyces cerevisiae
yeast
CT Drug Descriptors:
beta 1,3 glucan: EC, endogenous compound
beta 1,6 glucan: EC, endogenous compound
*cell membrane protein: EC, endogenous compound
chitin: EC, endogenous compound
ergosterol: EC, endogenous compound
glycosylphosphatidylinositol: EC, endogenous compound
mannoprotein: EC, endogenous compound
nikkomycin: AN, drug analysis
pir protein: EC, endogenous compound
pyrrole derivative: AN, drug analysis
unclassified drug
RN (beta 1,3 glucan) 9051-97-2; (chitin) 1398-61-4; (ergosterol) 23637-22-1, 2418-45-3, 3992-98-1, 57-87-4; (nikkomycin) 86003-55-6

L135 ANSWER 11 OF 38 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
AN 1999360240 EMBASE Full-text
TI Antifungal activities of antineoplastic agents: Saccharomyces cerevisiae as a model system to study drug action.
AU Cardenas, Maria E.; Cruz, M. Cristina; Heitman, Joseph (correspondence)
CS Department of Genetics, Duke University Medical Center, Durham, NC, United States. heitm001@duke.edu
AU Del Poeta, Maurizio; Perfect, John R.; Heitman, Joseph (correspondence)
CS Department of Medicine, Duke University Medical Center, Durham, NC, United States. heitm001@duke.edu
AU Chung, Namjin; Heitman, Joseph (correspondence)
CS Dept. of Pharmacol. and Cancer Biol., Duke University Medical Center, Durham, NC, United States. heitm001@duke.edu
AU Perfect, John R.; Heitman, Joseph (correspondence)
CS Department of Microbiology, Duke University Medical Center, Durham, NC, United States. heitm001@duke.edu
AU Heitman, Joseph (correspondence)
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AU Heitman, Joseph (correspondence)
CS 322 CARL Building, Box 3546, Duke University Medical Center, Research Dr., Durham, NC 27710, United States. heitm001@duke.edu
SO Clinical Microbiology Reviews, (Oct 1999) Vol. 12, No. 4, pp. 583-611.
Refs: 361
ISSN: 0893-8512 CODEN: CMIREX
CY United States
DT Journal; General Review; (Review)
FS 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 29 Oct 1999
Last Updated on STN: 29 Oct 1999
ED Entered STN: 29 Oct 1999
Last Updated on STN: 29 Oct 1999
AB Recent evolutionary studies reveal that microorganisms including yeasts and fungi are more closely related to mammals than was previously appreciated. Possibly as a consequence, many natural-product toxins that have antimicrobial activity are also toxic to mammalian cells. While this makes it difficult to discover antifungal agents without toxic side effects, it also has enabled detailed studies of drug action in simple genetic model systems. We review here studies on the antifungal actions of antineoplasmic agents. Topics covered include the mechanisms of action of inhibitors of topoisomerases I and II; the immunosuppressants rapamycin, cyclosporin A, and FK506; the phosphatidylinositol 3-kinase inhibitor wortmannin; the angiogenesis inhibitors fumagillin and ovalicin; the HSP90 inhibitor geldanamycin; and agents that inhibit sphingolipid metabolism. In general, these natural products inhibit target proteins conserved from microorganisms to humans. These studies highlight the potential of microorganisms as screening tools to elucidate the mechanisms of action of novel pharmacological agents with unique effects against specific mammalian cell types, including neoplastic cells. In addition, this analysis suggests that antineoplastic agents and derivatives might find novel indications in the treatment of fungal infections, for which few agents are presently available, toxicity remains a serious concern, and drug resistance is emerging.
CT Medical Descriptors:
antifungal activity
drug mechanism
drug targeting
human
multidrug resistance
*mycosis: DR, drug resistance
*mycosis: DT, drug therapy
nonhuman
review
Saccharomyces cerevisiae
CT Drug Descriptors:
angiogenesis inhibitor: DT, drug therapy
angiogenesis inhibitor: PD, pharmacology
antiestrogen: DT, drug therapy
antiestrogen: PD, pharmacology
*antineoplastic agent: DT, drug therapy
*antineoplastic agent: PD, pharmacology
camptothecin: DT, drug therapy
camptothecin: PD, pharmacology
cisplatin: DT, drug therapy
cisplatin: PD, pharmacology
cyclosporin A: DT, drug therapy

cyclosporin A: PD, pharmacology
DNA topoisomerase inhibitor: DT, drug therapy
DNA topoisomerase inhibitor: PD, pharmacology
enzyme inhibitor: DT, drug therapy
enzyme inhibitor: PD, pharmacology
fumagillin: DT, drug therapy
fumagillin: PD, pharmacology
fumagillol chloroacetylcarbamate: DT, drug therapy
fumagillol chloroacetylcarbamate: PD, pharmacology
geldanamycin: DT, drug therapy
geldanamycin: PD, pharmacology
irinotecan: DT, drug therapy
irinotecan: PD, pharmacology
phosphodiesterase inhibitor: DT, drug therapy
phosphodiesterase inhibitor: PD, pharmacology
protein n myristoyltransferase
raloxifene: DT, drug therapy
raloxifene: PD, pharmacology
rapamycin: DT, drug therapy
rapamycin: PD, pharmacology
tacrolimus: DT, drug therapy
tacrolimus: PD, pharmacology
tamoxifen: DT, drug therapy
tamoxifen: PD, pharmacology
topotecan: DT, drug therapy
topotecan: PD, pharmacology
wortmannin: DT, drug therapy
wortmannin: PD, pharmacology

RN (camptothecin) 7689-03-4; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (cyclosporin A) 59865-13-3, 63798-73-2; (fumagillin) 23110-15-8; (fumagillol chloroacetylcarbamate) 129298-91-5; (geldanamycin) 30562-34-6; (irinotecan) 100286-90-6; (protein n myristoyltransferase) 110071-61-9; (raloxifene) 82640-04-8, 84449-90-1; (rapamycin) 53123-88-9; (tacrolimus) 104987-11-3; (tamoxifen) 10540-29-1; (topotecan) 119413-54-6, 123948-87-8; (wortmannin) 19545-26-7

CN fk 506; tnp 470

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AN 1999108640 EMBASE Full-text

TI Molecular modelling of lanosterol 14α-demethylase (CYP51) from Saccharomyces cerevisiae via homology with CYP102, a unique bacterial cytochrome P450 isoform: Quantitative structure-activity relationships (QSARs) within two related series of antifungal azole derivatives.

AU Lewis, David F. V. (correspondence); Wiseman, Alan
CS School of Biological Sciences, University of Surrey, Guildford, Surrey GU2 5XH, United Kingdom. d.lewis@surreyacuk; d.lewis@surrey.ac.uk
AU Tarbit, Mike H.
CS Glaxo Wellcome R. and D. Limited, Park Road, Ware, Hertfordshire, SG12 0DP, United Kingdom.

SO Journal of Enzyme Inhibition, (1999) Vol. 14, No. 3, pp. 175-192.
Refs: 45
ISSN: 8755-5093 CODEN: ENINEG
CY United Kingdom
DT Journal; Article

FS 029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology

LA English
SL English
ED Entered STN: 28 Apr 1999
Last Updated on STN: 28 Apr 1999
ED Entered STN: 28 Apr 1999
Last Updated on STN: 28 Apr 1999
AB The construction of a three-dimensional molecular model of the fungal form of cytochrome P450 (CYP51) from Saccharomyces cerevisiae, based on homology with the haemoprotein domain of CYP102 from Bacillus megaterium (a unique bacterial P450 of known crystal structure) is described. It is found that the endogenous substrate, lanosterol, can readily occupy the putative active site of the CYP51 model such that the known mono-oxygenation reaction, leading to C(14)-demethylation of lanosterol, is the preferred route of metabolism for this particular substrate. Key amino acid contacts within the CYP51 active site appear to orientate lanosterol for oxidative attack at the C(14)-methyl group, and the position of the substrate relative to the haem moiety is consistent with the phenyl-iron complexation studies reported by Tuck et al. Typical azole inhibitors, such as ketoconazole. are able to fit the putative active site of CYP51 by a combination of haem ligation, hydrogen bonding, π-π stacking and hydrophobic interactions within the enzyme's haem environment. The mode of action of azole antifungals, as described by the modelling studies, is supported by quantitative structure-activity relationship (QSAR) analyses on two groups of structurally related fungal inhibitors. Moreover, the results of molecular electrostatic isopotential (EIP) energy calculations are compatible with the proposed mode of binding between azole antifungal agents and the putative active site of CYP51, although membrane interactions may also have a role in the antifungal activity of azole derivatives.
CT Medical Descriptors:
antifungal activity
article
*bacillus megaterium
binding site
crystal structure
demethylation
electric potential
hydrogen bond
hydrophobicity
molecular model
nonhuman
oxygenation
priority journal
protein domain
*saccharomyces cerevisiae
sequence homology
*structure activity relation
CT Drug Descriptors:
antifungal agent
carbon 14
cytochrome p450
hemoprotein
ketoconazole
*lanosterol derivative
*pyrrole derivative
RN (carbon 14) 14762-75-5; (cytochrome P450) 9035-51-2; (ketoconazole) 65277-42-1

L135 ANSWER 13 OF 38 EMBASE
AN 1997120398 EMBASE Full-text
TI Sphingolipid synthesis as a target for antifungal drugs.

Complementation of the inositol phosphorylceramide synthase defect in a mutant strain of Saccharomyces cerevisiae by the AUR1 gene.

AU Nagiec, M. Marek; Nagiec, Elzbieta E.; Baltisberger, Julie A.; Wells, Gerald B.; Lester, Robert L.; Dickson, Robert C. (correspondence)
CS Department of Biochemistry, Lucille P. Markey Cancer Center, Univ. of Kentucky Medical Center, Lexington, KY 40536-0084, United States. bobd@pop.uky.edu
AU Dickson, Robert C. (correspondence)
CS Department of Biochemistry, Lucille P. Markey Cancer Center, Kentucky University Medical Center, Lexington, KY 40536-0084, United States. bobd@pop.uky.edu

SO Journal of Biological Chemistry, (11 Apr 1997) Vol. 272, No. 15, pp. 9809-9817.
Refs: 40
ISSN: 0021-9258 CODEN: JBCHA3
CY United States
DT Journal; Article
FS 037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 29 May 1997
Last Updated on STN: 29 May 1997
ED Entered STN: 29 May 1997
Last Updated on STN: 29 May 1997

AB We have identified a Saccharomyces cerevisiae gene necessary for the step in sphingolipid synthesis in which inositol phosphate is added to ceramide to form inositol -P-ceramide, a reaction catalyzed by phosphatidylinositol :ceramide phosphoinositol transferase (IPC synthase). This step should be an effective target for antifungal drugs. A key element in our experiments was the development of a procedure for isolating mutants defective in steps in sphingolipid synthesis downstream from the first step including a mutant defective in IPC synthase. An IPC synthase defect is supported by data showing a failure of the mutant strain to incorporate radioactive inositol or N-acetylsphinganine into sphingolipids and, by using an improved assay, a demonstration that the mutant strain lacks enzyme activity. Furthermore, the mutant accumulates ceramide when fed exogenous phytosphingosine as expected for a strain lacking IPC synthase activity. Ceramide accumulation is accompanied by cell death, suggesting the presence of a ceramide-activated death response in yeast. A gene , AUR1 (YKL004w), that complements the IPC synthase defect and restores enzyme activity and sphingolipid synthesis was isolated. Mutations in AUR1 had been shown previously to give resistance to the antifungal drug aureobasidin A, leading us to predict that the drug should inhibit IPC synthase activity. Our data show that the drug is a potent inhibitor of IPC synthase with an IC(50) of about 0.2 nM. Fungal pathogens are an increasing threat to human health. Now that IPC synthase has been shown to be the target for aureobasidin A, it should be possible to develop high throughput screens to identify new inhibitors of IPC synthase to combat fungal diseases.

CT Medical Descriptors:
*antifungal activity
article
bioaccumulation
biosynthesis
drug mechanism
enzyme activity
nonhuman
priority journal
saccharomyces cerevisiae

sequence homology
CT Drug Descriptors:
*antifungal agent: PD, pharmacology
*aureobasidin a: DV, drug development
*aureobasidin a: PD, pharmacology
*inositol phosphorylceramide synthase
*myoinositol 1 phosphate synthase
*sphingolipid: EC, endogenous compound
unclassified drug
RN (aureobasidin A) 127785-64-2; (myoinositol 1 phosphate synthase) 9032-95-5

L135 ANSWER 14 OF 38 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
AN 1997374373 EMBASE Full-text
TI In silicio identification of glycosyl-phosphatidylinositol-anchored plansma-membrane and cell wall proteins of Saccharomyces cerevisiae.
AU Caro, L. Heleen P.; Vossen, Jack H.; Ram, Arthur F. J.; Van Den Ende, Herman; Klis, Frans M.
CS Fungal Cell Wall Group Amsterdam, BioCentrum Amsterdam, University of Amsterdam, Kruislaan 318, 1098 SM Amsterdam, Netherlands.
AU Tettelin, Herve
CS U. de Biochimie Physiologique, Univ. Catholique de Louvain, Place Croix du Sud, 2120, 1348 Liuvain-La-Neuve, Belgium.
AU Caro, L. Heleen P.
CS Institute for Molecular Cell Biology, BioCentrum Amsterdam, University of Amsterdam, Kruislaan 318, 1098 SM Amsterdam, Netherlands.
AU Caro, H.L.P. (correspondence)
CS Institute Molecular Cell Biology, BioCentrum Amsterdam, University of Amsterdam, Kruislaan 318, 1098 SM Amsterdam, Netherlands.
SO Yeast, (Dec 1997) Vol. 13, No. 15, pp. 1477-1489.
Refs: 65
ISSN: 0749-503X CODEN: YESTE3
CY United Kingdom
DT Journal; Article
FS 037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English; English
SL English
ED Entered STN: 18 Dec 1997
Last Updated on STN: 18 Dec 1997
ED Entered STN: 18 Dec 1997
Last Updated on STN: 18 Dec 1997
AB Use of the Von Heijne algorithm allowed the identification of 686 open reading frames (ORFs) in the genome of Saccharomyces cerevisiae that encode proteins with a potential N-terminal signal sequence for entering the secretory pathway. On further analysis, 51 of these proteins contain a potential glycosyl-phosphatidylinositol (GPI)-attachment signal. Seven additional ORFs were found to belong to this group. Upon examination of the possible GPI-attachment sites, it was found that in yeast the most probable amino acids for GPI-attachment are asparagine and glycine. In yeast, GPI-proteins are found at the cell surface, either attached to the plasma-membrane or as an intrinsic part of the cell wall . It was noted that plasma-membrane GPI-proteins possess a dibasic residue motif just before their predicted GPI -attachment site. Based on this, and on homologies between proteins, families of plasma-membrane and cell wall proteins were assigned, revealing 20 potential plasma-membrane and 38 potential cell wall proteins. For members of three plasma-membrane protein families, a function has been described. On the other hand,

most of the cell wall proteins seem to be structural components of the wall, responsive to different growth conditions. The GPI-attachment site of yeast slightly differs from mammalian cells. This might be of use in the development of anti-fungal drugs.

CT Medical Descriptors:
article
controlled study
nonhuman
open reading frame
priority journal
protein degradation
*saccharomyces cerevisiae
CT Drug Descriptors:
*antifungal agent: DV, drug development
*cell membrane protein: EC, endogenous compound
*glypican: EC, endogenous compound

L135 ANSWER 15 OF 38 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
AN 1996180608 EMBASE Full-text
TI Missense mutations at the FKBP12-rapamycin-binding site of TOR1.
AU Freeman, Katie; Livi, George P., Dr. (correspondence)
CS Dept. of Gene Expression Sciences, SmithKline Beecham Pharmaceuticals, King of Prussia, PA 19406, United States. george-p-livi@sbphrd.com
AU Livi, George P., Dr. (correspondence)
CS Dept. of Gene Expression Sciences, UE0548, SmithKline Beecham Pharmaceuticals, King of Prussia, PA 19406, United States. george-p-livi@sbphrd.com
AU Livi, George P., Dr. (correspondence)
CS Department Gene Expression Sciences, SmithKline Beecham Pharmaceuticals, King of Prussia, PA 19406, United States.
SO Gene, (12 Jun 1996) Vol. 172, No. 1, pp. 143-147.
Refs: 20
ISSN: 0378-1119 CODEN: GENED6
CY Netherlands
DT Journal; Article
FS 037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 8 Jul 1996
Last Updated on STN: 8 Jul 1996
ED Entered STN: 8 Jul 1996
Last Updated on STN: 8 Jul 1996
AB The TOR genes were first identified in Saccharomyces cerevisiae by the isolation of mutants which exhibit dominant resistance to the immunosuppressive and antifungal drug rapamycin (Rm). The originally characterized Rm-resistant (Rm(R)) TOR1-1 and TOR2-1 alleles contain an Arg in place of a conserved Ser residue, which lies adjacent to the phosphatidylinositol (PI) kinase-related domain of TOR (Ser(1972) in TOR1; Ser(1975) in TOR2). Additional spontaneous Rm(R) mutants containing Lys, Ile or Asn substitutions were subsequently isolated. As this Ser is a potential site for protein kinase C phosphorylation, we were interested in determining whether the observed Rm(R) is due to steric hindrance of the FKBP12-Rm-TOR interaction or whether phosphorylation at this site is required to mediate the interaction. Using site-directed mutagenesis, we replaced the Ser(1972) residue of TOR1 with either a conservative residue, Ala, an alternative potential phosphorylation site, Thr, or Asp to mimic phosphorylation. The TOR1(S1972A) mutant protein retained Rm sensitivity (Rm(S)), whereas both the Thr and Asp substitutions conferred Rm(R). Rm(S) correlated with the ability

to interact with FKBP12-Rm in a two-hybrid assay: both wild-type TOR1 and the S1972A mutant retained the ability to interact with FKBP12-Rm, whereas the S1972T, S1972D and S1972R mutants failed to interact. All mutant TOR1 proteins were able to complement the growth defect of tor1 null alleles, suggesting that the Ser(1972) residue may not be required for TOR1 function in cycling cells. Since a TOR1(S1972A) mutant protein confers a Rm(S) phenotype, interacts with FKBP12-Rm in a two-hybrid assay, and functions in vivo, we conclude that phosphorylation at Ser(1972) is not necessary for the interaction between TOR1 and FKBP12-Rm.

CT Medical Descriptors:
amino acid substitution
article
controlled study
drug binding site
drug resistance
enzyme phosphorylation
*missense mutation
nonhuman
priority journal
*saccharomyces cerevisiae
site directed mutagenesis

CT Drug Descriptors:
antifungal agent
arginine: EC, endogenous compound
aspartic acid: EC, endogenous compound
phosphatidylinositol kinase: EC, endogenous compound
protein kinase c: EC, endogenous compound
*rapamycin
serine: EC, endogenous compound
threonine: EC, endogenous compound

RN (arginine) 1119-34-2, 15595-35-4, 7004-12-8, 74-79-3; (aspartic acid) 56-84-8, 6899-03-2; (phosphatidylinositol kinase) 37205-54-2; (protein kinase C) 141436-78-4; (rapamycin) 53123-88-9; (serine) 56-45-1, 6898-95-9; (threonine) 36676-50-3, 72-19-5

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AN 1994202694 EMBASE Full-text

TI A conditionally lethal yeast mutant blocked at the first step in glycosyl phosphatidylinositol anchor synthesis.

AU Orlean, Peter (correspondence)

CS Dept. of Biochemistry, 309 Roger Adams Laboratory, Univ. Illinois at Urbana-Champaign, 600 South Mathews Ave., Urbana, IL 61801, United States.

AU Leidich, Steven D.; Drapp, Darren A.; Orlean, Peter (correspondence)

CS Department of Biochemistry, Univ. Illinois at Urbana-Champaign, Urbana, IL 61801, United States.

AU Orlean, Peter (correspondence)

CS 309 Roger Adams Laboratory, Dept. of Biochemistry, University of Illinois, 600 South Mathews Ave., Urbana, IL 61801, United States.

SO Journal of Biological Chemistry, (8 Apr 1994) Vol. 269, No. 14, pp. 10193-10196.
Refs: 38
ISSN: 0021-9258 CODEN: JBCHA3

CY United States

DT Journal; Article

FS 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology

LA English

SL English

ED Entered STN: 27 Jul 1994

Last Updated on STN: 27 Jul 1994
ED Entered STN: 27 Jul 1994
Last Updated on STN: 27 Jul 1994
AB Glycosyl phosphatidylinositols (GPIs) anchor many proteins to the surface of eukaryotic cells and may also serve as sorting signals on proteins and participate in signal transduction. We have isolated a Saccharomyces cerevisiae GPI anchoring mutant, gpi1, using a colony screen for cells blocked in [(3)H]inositol incorporation into protein. The gpi1 mutant is defective in vitro in the synthesis of N-acetylglucosaminyl phosphatidylinositol, the first intermediate in GPI synthesis, and is also temperature-sensitive for growth. Completion of the first step in GPI assembly is therefore required for growth of the unicellular eukaryote S. cerevisiae. GPI synthesis could therefore be exploited as a target for antifungal or antiparasitic agents.
CT Medical Descriptors:
article
enzyme activity
enzyme assay
fungus growth
fungus mutant
isotope labeling
nonhuman
priority journal
*protein synthesis
saccharomyces cerevisiae
temperature sensitivity
yeast cell
CT Drug Descriptors:
carbon 14
dolichol phosphate
*fungal protein
gene product
*glycosylphosphatidylinositol
inositol
lipid
methionine
sulfur 35
tritium
uridine diphosphate n acetylglucosamine
RN (carbon 14) 14762-75-5; (dolichol phosphate) 12698-55-4, 34457-14-2; (inositol) 55608-27-0, 6917-35-7, 87-89-8; (lipid) 66455-18-3; (methionine) 59-51-8, 63-68-3, 7005-18-7; (sulfur 35) 15117-53-0; (tritium) 10028-17-8; (uridine diphosphate n acetylglucosamine) 528-04-1

L135 ANSWER 17 OF 38 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
AN 1994373373 EMBASE Full-text
TI Import of phosphatidylinositol and phosphatidylcholine into mitochondria of the yeast, Saccharomyces cerevisiae.
AU Lampl, Manfred
CS Institut fur Biochemie und Lebensmittelchemie, Technische Universitat Graz, Petersgasse 1212, A-8010 Graz, Austria.
AU Daum, G. (correspondence)
CS Inst. Biochemie/Lebensmittelchemie, Technische Universitat Graz, Petersgasse 12/2, A-8010 Graz, Austria.
SO FEBS Letters, (1994) Vol. 356, No. 1, pp. 1-4.
ISSN: 0014-5793 CODEN: FEBLAL
CY Netherlands
DT Journal; Article
FS 037 Drug Literature Index

004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 12 Jan 1995
Last Updated on STN: 12 Jan 1995
ED Entered STN: 12 Jan 1995
Last Updated on STN: 12 Jan 1995
AB An in vitro assay was designed to study the import of (3)H-labeled phosphatidylinositol and phosphatidylcholine, respectively, from unilamellar vesicles into isolated mitochondria of the yeast, Saccharomyces cerevisiae. Both phospholipids reached the inner mitochondrial membrane. During import they were detected in contact sites between the outer and the inner mitochondrial membrane, supporting the notion that these zones are sites of intramitochondrial phospholipid transport. The uncoupler CCCP, the antibiotic adriamycin, and energy depletion caused by oligomycin and apyrase did not inhibit the transport of phosphatidylinositol and phosphatidylcholine into mitochondria.
CT Medical Descriptors:
article
controlled study
*intracellular transport
*mitochondrion
nonhuman
*phospholipid transfer
priority journal
*Saccharomyces cerevisiae
uncoupler: TO, drug toxicity
CT Drug Descriptors:
apyrase: CB, drug combination
doxorubicin: PD, pharmacology
oligomycin: CB, drug combination
oligomycin: PD, pharmacology
*phosphatidylcholine
*phosphatidylinositol
unclassified drug
RN (apyrase) 9000-95-7; (doxorubicin) 23214-92-8, 25316-40-9; (oligomycin) 1404-19-9; (phosphatidylcholine) 55128-59-1, 8002-43-5

L135 ANSWER 18 OF 38 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
AN 1993292610 EMBASE Full-text
TI Dominant missense mutations in a novel yeast protein related to mammalian phosphatidylinositol 3-kinase and VPS34 abrogate rapamycin cytotoxicity.
AU Cafferkey, R.; Young, P.R.; McLaughlin, M.M.; Bergsma, D.J.; Koltin, Y.; Sathe, G.M.; Faucette, L.; Eng, W.-K.; Johnson, R.K.; Livi, G.P. (correspondence)
CS Gene Expression Sciences Department, SmithKline Beecham Pharmaceuticals, King of Prussia, PA 19406, United States.
SO Molecular and Cellular Biology, (1993) Vol. 13, No. 10, pp. 6012-6023. ISSN: 0270-7306 CODEN: MCEBD4
CY United States
DT Journal; Article
FS 029 Clinical and Experimental Biochemistry
037 Drug Literature Index
LA English
SL English
ED Entered STN: 31 Oct 1993
Last Updated on STN: 31 Oct 1993
ED Entered STN: 31 Oct 1993

Last Updated on STN: 31 Oct 1993

AB Rapamycin is a macrolide antifungal agent that exhibits potent immunosuppressive properties. In Saccharomyces cerevisiae, rapamycin sensitivity is mediated by a specific cytoplasmic receptor which is a homolog of human FKBP12 (hFKBP12). Deletion of the gene for yeast FKBP12 (RBP1) results in recessive drug resistance, and expression of hFKBP12 restores rapamycin sensitivity. These data support the idea that FKBP12 and rapamycin form a toxic complex that corrupts the function of other cellular proteins. To identify such proteins, we isolated dominant rapamycin-resistant mutants both in wild-type haploid and diploid cells and in haploid rbp1::URA3 cells engineered to express hFKBP12. Genetic analysis indicated that the dominant mutations are nonallelic to mutations in RBP1 and define two genes, designated DRR1 and DRR2 (for dominant rapamycin resistance). Mutant copies of DRR1 and DRR2 were cloned from genomic YCp50 libraries by their ability to confer drug resistance in wild-type cells. DNA sequence analysis of a mutant drr1 allele revealed a long open reading frame predicting a novel 2470- amino-acid protein with several motifs suggesting an involvement in intracellular signal transduction, including a leucine zipper near the N terminus, two putative DNA-binding sequences, and a domain that exhibits significant sequence similarity to the 110-kDa catalytic subunit of both yeast (VPS34) and bovine phosphatidylinositol 3-kinases. Genomic disruption of DRR1 in a mutant haploid strain restored drug sensitivity and demonstrated that the gene encodes a nonessential function. DNA sequence comparison of seven independent drr1(dom) alleles identified single base pair substitutions in the same codon within the phosphatidylinositol 3-kinase domain, resulting in a change of Ser-1972 to Arg or Asn. We conclude either that DRR1 (alone or in combination with DRR2) acts as a target of FKBP12-rapamycin complexes or that a missense mutation in DRR1 allows it to compensate for the function of the normal drug target.

CT Medical Descriptors:
amino acid sequence
article
chromosome map
*cytotoxicity
DNA sequence
drug resistance
*drug sensitivity
  fungus mutant
  *gene mutation
molecular cloning
nonhuman
polymerase chain reaction
priority journal
  restriction mapping
  RNA analysis
  Saccharomyces cerevisiae
signal transduction

CT Drug Descriptors:
  *cell protein: EC, endogenous compound
cyclosporin A
*cytoplasmic receptor
DNA: EC, endogenous compound
  *phosphatidylinositol kinase
*rapamycin
tacrolimus

RN (cyclosporin A) 59865-13-3, 63798-73-2; (DNA) 9007-49-2; (phosphatidylinositol kinase) 37205-54-2; (rapamycin) 53123-88-9; (tacrolimus) 104987-11-3

CN (1) fk 506

CO (1) smith kline beecham (United Kingdom); sandoz (United States)

GEN GENBANK L19540 submitted number

L135 ANSWER 19 OF 38 DRUGU COPYRIGHT 2009 THOMSON REUTERS on STN
AN 1999-20718 DRUGU M Full-text
TI LY303366 exhibits rapid and potent fungicidal activity in flow cytometric assays of yeast viability.
AU Green L J; Marder P; Mann L L; Chio L C; Current W L
CS Lilly
LO Indianapolis, Ind., USA
SO Antimicrob.Agents Chemother. (43, No. 4, 830-35, 1999) 4 Fig. 3 Tab. 31 Ref.
CODEN: AMACCQ ISSN: 0066-4804
AV DC0444, Lilly Corporate Center, Indianapolis, IN 46285, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The fungicidal activity of LY-303366 (Lilly) was compared with that of amphotericin B (AMB, Sigma-Chemical) and cilofungin (Lilly) using flow cytometric assays of the viability of Candida albicans and Sacch. cerevisiae, and cell sorting. The results suggest that LY-303366 is potent and fast-acting, particularly against actively growing yeasts, and may be clinically useful.
AN 1999-20718 DRUGU M Full-text
M Microbiology
23 Antimicrobials
55 Fungicides
73 Trial Preparations
CT [01] LY-303366 *PH; LILLY *FT; LY-303366 *RN; CANDIDA *FT; ALBICANS *FT; SACCH. *FT; CEREVISIAE *FT; FUNGICIDE *FT; ANTIBIOTIC *FT; SCREENING-METHOD *FT; FUNGUS *FT; TRIAL-PREP. *FT; FUNGICIDES *FT; PROTOZOACIDES *FT; ANTIBIOTICS *FT; COCCIDIOSTATICS *FT; PH *FT

L135 ANSWER 20 OF 38 DRUGU COPYRIGHT 2009 THOMSON REUTERS on STN
AN 1994-19564 DRUGU M Full-text
TI Rapid determination of antifungal activity by flow cytometry.
AU Green L; Petersen B; Steimel L; Haeber P; Current W
CS Lilly
LO Indianapolis, Indiana, United States
SO J.Clin.Microbiol. (32, No. 4, 1088-91, 1994) 1 Fig. 3 Tab. 25 Ref.
CODEN: JCMIDW ISSN: 0095-1137
AV Lilly Laboratories for Clinical Research, Wishard Memorial Hospital, 1001 W. 10th Street, Indianapolis, IN 46202, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB A rapid assay of antifungal activity, utilizing flow cytometry was developed, the detection of propidium iodide (PI, Sigma-Chemical) in drug damaged cells was involved. Organisms involved included Candida albicans A26 and SC5314, C. tropicalis CT5, C. parapsilosis CP5 and CP8, Cryptococcus neoformans M1-106 and Saccharomyces cerevisiae DBY746 with the antifungal agents cilofungin (CF), LY-295337 (both Takara), fluconazole (FC, Pfizer) and amphotericin-b (AB, Sigma-Chemical). Flow cytometry may provide an improved, rapid method for determining and comparing antifungal activities of compounds with differing modes of action.
AN 1994-19564 DRUGU M Full-text
M Microbiology

23 Antimicrobials
55 Fungicides
73 Trial Preparations

CT PROPIDIUM *RC; IN-VITRO *FT; SCREENING-METHOD *FT; FUNGICIDE *FT; FLOW-CYTOMETRY *FT; SIGMA-CHEM. *FT; CANDIDA *FT; ALBICANS *FT; TROPICALIS *FT; PARAPSILOSIS *FT; CRYPTOCOCCUS *FT; NEOFORMANS *FT; SACCH. *FT; YEAST *FT; CEREVISIAE *FT; FUNGUS *FT; FUNGUS *FT

[01] CILOFUNGIN *PH; LY-121019 *RN; TAKARA *FT; ANTIBIOTICS *FT; FUNGICIDES *FT; PH *FT
RN: 79404-91-4

[02] LY-295337 *PH; LY-295337 *RN; TRIAL-PREP. *FT; FUNGICIDES *FT; TAKARA *FT; PH *FT

[03] FLUCONAZOLE *PH; PFIZER *FT; FLUCONAZO *RN; FUNGICIDES *FT; PH *FT
RN: 86386-73-4

[04] AMPHOTERICIN-B *PH; SIGMA-CHEM. *FT; AMPHOTERI *RN; ANTIBIOTICS *FT; FUNGICIDES *FT; PH *FT
RN: 1397-89-3

L135 ANSWER 21 OF 38 LIFESCI COPYRIGHT 2009 CSA on STN
AN 1998:23938 LIFESCI Full-text
TI Phosphoinositolglycan-peptides from yeast potently induce metabolic insulin actions in isolated rat adipocytes, cardiomyocytes, and diaphragms
AU Mueller, G.; Wied, S.; Crecelius, A.; Kessler, A.; Eckel, J.
CS Hoechst AG, Hoechst-Marion-Roussel, Res. Site Frankfurt, DG Metabolic Dis., Bldg. H825, D-65926 Frankfurt a.m., FRG
SO ENDOCRINOLOGY, (19970800) vol. 138, no. 8.
ISSN: 0013-7227.
DT Journal
FS K
LA English
SL English
AB Polar headgroups of free glycosyl-phosphatidylinositol (GPI) lipids or protein-bound GPI membrane anchors have been shown to exhibit insulin-mimetic activity in different cell types. However, elucidation of the molecular mode of action of these phospho-inositolglycan (PIG) molecules has been hampered by 1) lack of knowledge of their exact structure; 2) variable action profiles; and 3) rather modest effects. In the present study, these problems were circumvented by preparation of PIG-peptides (PIG-P) in sufficient quantity by sequential proteolytic (V8 protease) and lipolytic (phosphatidylinositol-specific phospholipase C) cleavage of the GPI-anchored plasma membrane protein, Gce1p, from the yeast Saccharomyces cerevisiae. The structure of the resulting PIG-P, NH sub(2)-Tyr-Cys-Asn-ethanolamine-PO sub(4)-6(Man1-2)Man1-2Man1-6Man1-4Glc NH sub(2)1-6myo-inositol-1,2-cyclicPO sub(4), was revealed by amino acid analysis and Dionex exchange chromatography of fragments generated enzymatically or chemically from the neutral glycan core and is in accordance with the known consensus structures of yeast GPI anchors. PIG-P stimulated glucose transport and lipogenesis in normal, desensitized and receptor-depleted isolated rat adipocytes, increased glycerol-3-phosphate acyltransferase activity and translocation of the glucose transporter isoform 4, and inhibited isoproterenol-induced lipolysis and protein kinase A activation in adipocytes. Furthermore, PIG-P was found to stimulate glucose transport in isolated rat cardiomyocytes and glycogenesis and glycogen synthase in isolated rat diaphragms. The concentration-dependent effects of the PIG-P reached 70-90% of the maximal insulin activity with EC sub(50)-values of 0.5-5 mu M. Chemical or enzymic cleavages within the glycan or peptide portion of the PIG-P led to decrease or loss of activity. The data demonstrate that PIG-P exhibits a potent insulin-mimetic activity which covers

a broad spectrum of metabolic insulin actions on glucose transport and metabolism.
CC 03100 Miscellaneous topics
UT Saccharomyces cerevisiae; insulin; glucose transport; mimetic activity

L135 ANSWER 22 OF 38 LIFESCI COPYRIGHT 2009 CSA on STN
AN 97:8259 LIFESCI Full-text
TI Candida albicans phosphatidylinositol synthase has common features with both Saccharomyces cerevisiae and mammalian phosphatidylinositol synthases
AU Antonsson, B.E.; Klig, L.S.
CS Glaxo Inst. for Mol. Biol., 14 Chemin des Aulx, CH-1228 Plan-les Ouates, Geneva, Switzerland
SO YEAST, (1996) vol. 12, no. 5, pp. 449-456.
ISSN: 0749-503X.
DT Journal
FS K
LA English
SL English
AB Phosphatidylinositol (PI) synthase (cytidine 5'-diphospho (CDP)-1,2-diacyl-sn-glycerol:myo-inositol 3-phosphatidyltransferase, EC 2.7.8.11) was isolated from the microsomal cell fraction of Candida albicans. The Triton X-100 extracted enzyme was enriched 140-fold by affinity chromatography on CDP-diacylglycerol-Sepharose. The enzyme had a pH optimum at 9.5 in glycine/NaOH buffer. It had an absolute requirement for Mg super(2+) or Mn super(2+) and was inhibited by Ca super(2+) and Zn super(2+). Maximal activity was at 0.2-0.6 mM-CDP-diacylglycerol, higher concentrations inhibited the enzyme. With 2'-deoxy-CDP-diacylglycerol as the lipid substrate, optimal activity was at 0.7 mM. The K sub(m) for myo-inositol was determined to be 0.55 mM. The optimal temperature for the PI synthase reaction was 55 degree C. The C. albicans PI synthase shows differences to the Saccharomyces cerevisiae enzyme, such as activation by bivalent cations, inhibition by nucleotides, temperature optimum and activation energy, but also to the human PI synthase in preference for the lipid substrates, inhibition by nucleoside monophosphates and stabilization by Mn super(2+) and phospholipids.
CC 03020 Fungi
UT Candida albicans; phosphatidylinositol synthase; Saccharomyces cerevisiae; inositol

L135 ANSWER 23 OF 38 LIFESCI COPYRIGHT 2009 CSA on STN
AN 82:6358 LIFESCI Full-text
TI Purification of Yeast Hexokinase Isoenzymes Using Affinity Chromatography and Chromatofocusing.
AU Kopetzki, E.; Entian, K.-D.
CS Physiol. Chem. Inst., Univ. Tuebingen, Hoppe-Seyler-Str. 1, D-7400 Tuebingen, FRG
SO ANAL. BIOCHEM., (1982) vol. 121, no. 1, pp. 181-185.
DT Journal
FS L; K; A
LA English
SL English
AB A new procedure has been devised for the rapid isolation of Saccharomyces cerevisiae hexokinase isoenzymes PI and PII, giving specific activities comparable to those obtained after conventional purification. Hexokinases were bound to D-glucosamine, which had been coupled to CH Sepharose 4B using 6-aminohexanoic acid as a spacer. An ATP/D-glucose/MgCl sub(2) solution was used for elution. After concentration with DEAE-Sephacel, isoenzymes were separated by chromatofocusing. Hexokinase PI gave a single band on polyacrylamide gel electrophoresis, whereas one minor foreign band was seen for hexokinase PII.
CC 16002 Purification & preliminary characterization of peptides & proteins; 03020 Fungi; 01006 Enzymes & cofactors

UT hexokinase; isoenzymes; purification; Saccharomyces cerevisiae; affinity chromatography

L135 ANSWER 24 OF 38 BIOTECHDS COPYRIGHT 2009 THOMSON REUTERS on STN
AN 1986-09781 BIOTECHDS Full-text
TI Increased hydrophobicity of the P1' binding site in carboxypeptidase Y obtained by site-directed mutagenesis;
production of enzymes of biotechnological interest
AU Winther J R; Kielland-Brandt M C; Breddam K
LO Department of Chemistry, Carlsberg Laboratory, Gamle Carlsberg Vej 10, DK-2500 Copenhagen Valby, Denmark.
SO Carlsberg Res.Commun.; (1985) 50, 5, 273-84
CODEN: CRCODS
DT Journal
LA English
AB Chemical modification of Met-398 in Saccharomyces cerevisiae carboxypeptidase Y affects the enzyme specificity with respect to the Pi' position. For analysis of the role of Met-398, this residue was substituted by a leucyl residue using site-directed mutagenesis. Mutagenesis was performed in phage M13 on a subcloned fragment of PRc1, the structural gene for carboxypeptidase Y, using a dodecanucleotide containing the desired mutation as primer for secondary strand synthesis in vitro. A clone was identified in which codon 398 of the carboxypeptidase Y gene had mutated from ATG to TTG. This sequence was reintroduced into the original PRC1 gene context and a lambda-prc1 yeast strain was transformed with the resulting plasmid DNA. The mutant enzyme, Leu-398-carboxypeptidase Y, was isolated by affinity chromatography, and had the same mol.weight, N-terminal amino acid sequence and sugar content as carboxypeptidase Y. More drastic mutations at the Pi' position may be performed to produce enzymes of potential biotechnological interest. (30 ref)
AN 1986-09781 BIOTECHDS Full-text
CC A MICROBIOLOGY; A1 Genetics
CT SACCHAROMYCES CEREVISIAE CARBOXYPEPTIDASE-Y CHARACTERIZATION, ENZYME SPECIFICITY, SITE-DIRECTED MUTAGENESIS, APPL. TO ENZYME ENGINEERING FUNGUS

L135 ANSWER 25 OF 38 BIOTECHDS COPYRIGHT 2009 THOMSON REUTERS on STN
AN 1982-02496 BIOTECHDS Full-text
TI Preparation of phosphatidyl(2-3H)inositol from yeast grown in medium containing MYO(2-3H)inositol;
a simple and convenient method for obtaining radioisotope labeled phosphatidylinositol using Saccharomyces cerevisiae for use as a suitable substrate for phospholipase C
AU Graff G; Harlan J; Nanas N
LO University of Illinois at the Medical Center, Department of Biological Chemistry, Chicago, Illinois, U.S.A.
SO Prep.Biochem.; (1982) 12, 175-95
CODEN: PRBCBQ
DT Journal
LA English
AB A method for isolating and purifying phosphatidyl-(2-3H) inositol (3H)-(PI) from Saccharomyces cerevisiae is described. Lipids were extracted from cell pellets of S. cerevisiae (wild type YSC-2) incubated in a synthetic inositol-deficient medium containing myo-(2-3H)-inositol. (3H)-PI Was purified from yeast lipid extracts by medium pressure liquid chromatography on a silicic acid column. Degradation of PI was achieved with a partially purified preparation of a phosphatidyl-specific phospholipase C13 from human platelets. 95% Of the (3H)-inositol taken up by the cells was extractable by an organic solvent and 8% of the radio-isotope was incorporated into phosphatidylinositol. Palmitate represented the bulk of the saturated fatty

acid chains of the purified (2-3H)-PI following transesterification with sulfuric acid in methanol. Equi-molar quantities of unlabeled 1,2-diacylglycerol and phosphoryl(2-3H)inositol were formed from a mixture of yeast and soybean PI, which indicated that phospholipase C from human platelets does not recognize differences in the fatty acyl moeity of PI. (17 ref)
AN 1982-02496 BIOTECHDS Full-text
CC K BIOCATALYSIS; K1 Isolation and Characterization
CT RADIOLABELED PHOSPHATIDYLINOSITOL PREP., PURIFICATION SACCH. CEREVISIAE

L135 ANSWER 26 OF 38 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 1999:224142 SCISEARCH Full-text
GA The Genuine Article (R) Number: 176PA
TI Phosphatidylinositol synthesis in mycobacteria
AU Salman M (Reprint)
CS SmithKline Beecham Pharmaceut, 1250 S Collegeville Rd, POB 5089, Collegeville, PA 19426 USA (Reprint)
AU Lonsdale J T; Besra G S; Brennan P J
CS SmithKline Beecham Pharmaceut, Collegeville, PA 19426 USA; Colorado State Univ, Dept Microbiol, Ft Collins, CO 80523 USA; Univ Newcastle Upon Tyne, Sch Microbiol Immunol & Virol Sci, Newcastle Upon Tyne NE2 4HN, Tyne & Wear, England
CYA USA; England
SO BIOCHIMICA ET BIOPHYSICA ACTA-MOLECULAR AND CELL BIOLOGY OF LIPIDS, (4 JAN 1999) Vol. 1436, No. 3, pp. 437-450.
ISSN: 1388-1981.
PB ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
DT Article; Journal
LA English
REC Reference Count: 39
ED Entered STN: 1999
Last Updated on STN: 1999
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
ED Entered STN: 1999
Last Updated on STN: 1999
AB The metabolism and synthesis of an important mycobacterial lipid component, phosphatidylinositol (PI), and its metabolites, was studied in Mycobacterium smegmatis and M. smegmatis subcellular fractions. Little is known about the synthesis of PI in prokaryotic cells. Only a cell wall fraction (P60) in M. smegmatis was shown to possess PI synthase activity. Product was identified as PI by migration on TLC, treatment with phospholipase C and ion exchange chromatography. PI was the only major product (92.3%) when both cells and P60 fraction were labeled with [H-3]inositol. Also, a neutral lipid inositol-containing product (4.1% of the total label) was identified in the P60 preparations. Strangely, PI synthase substrates, CDP-dipalmitoyl-DAG and CDP-NBD-DAG, added to the assay did not stimulate [H-3]PI and NBD-PI yield by M. smegmatis. At the same time, addition of both substrates to rat liver and saccharomyces cerevisiae PI synthase assays resulted in an increase in the product yield. Upon addition of CHAPS to the mycobacterial PI synthase assay, both substrates were utilized in a dose-dependent manner for the synthesis of NBD-PI and [H-3]PI. These results demonstrate a strict substrate specificity of mycobacterial PI synthase toward endogenous substrates, K-m of the enzyme toward inositol was shown to be 25 mu M: Mg2+ stimulated the enzyme to a greater degree than Mn2+. Structural analogs of myo-inositol, epi-inositol and scyllo-inositol and Zn2+ were shown to be more potent inhibitors of mycobacterial PI synthase than of mammalian analogs. Lack of sequence homology with mammalian PI synthases, different kinetic characteristics, existence of selective inhibitors and an important physiological role in

mycobacteria, suggest that PI synthase may be a good potential target for antituberculosis therapy. (C) 1999 Elsevier Science B.V. All rights reserved.

CC BIOCHEMISTRY & MOLECULAR BIOLOGY; BIOPHYSICS; CELL BIOLOGY

ST Author Keywords: mycobacteria; phosphatidylinositol; phosphatidylinositol synthase; phosphatidylinositol mannoside; fluorescent lipid

STP KeyWords Plus (R): ARACHIDONOYL-DIACYLGLYCEROL KINASE; CELL-WALL; SACCHAROMYCES-CEREVISIAE; BIOSYNTHESIS; MEMBRANE; SYNTHASE; PURIFICATION; LIPOARABINOMANNAN; OLIGOSACCHARIDE; TUBERCULOSIS
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L135 ANSWER 27 OF 38 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 1997:553645 SCISEARCH Full-text

GA The Genuine Article (R) Number: XL842

TI Phosphoinositolglycan-peptides from yeast potently induce metabolic insulin actions in isolated rat adipocytes, cardiomyocytes, and diaphragms

AU Muller G (Reprint)

CS HOECHST AG, RES SITE FRANKFURT, DG METAB DIS, HOECHST MARION ROUSSEL, BLDG H825, D-65926 FRANKFURT, GERMANY (Reprint)

AU Wied S; Crecelius A; Kessler A; Eckel J

CS DIABET RES INST, MOL CARDIOL LAB, D-40225 DUSSELDORF, GERMANY

CYA GERMANY

SO ENDOCRINOLOGY, (AUG 1997) Vol. 138, No. 8, pp. 3459-3475.
ISSN: 0013-7227.

PB ENDOCRINE SOC, 4350 EAST WEST HIGHWAY SUITE 500, BETHESDA, MD 20814-4110.

DT Article; Journal

FS LIFE

LA English

REC Reference Count: 58

ED Entered STN: 1997
Last Updated on STN: 1997
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

ED Entered STN: 1997
Last Updated on STN: 1997

AB Polar headgroups of free glycosyl-phosphatidylinositol (GPI) lipids or protein-bound GPI membrane anchors have been shown to exhibit insulin-mimetic activity in different cell types. However, elucidation of the molecular mode of action of these phospho-inositolglycan (PIG) molecules has been hampered by 1) lack of knowledge of their exact structure; 2) variable action profiles; and 3) rather modest effects. In the present study, these problems were circumvented by preparation of PIG-peptides (PIG-P) in sufficient quantity by sequential proteolytic (V8 protease) and lipolytic (phosphatidylinositol-specific phospholipase C) cleavage of the GPI-anchored plasma membrane protein, Gce1p, from the yeast Saccharomyces cerevisiae. The structure of the resulting PIG-P, NH2-Tyr-Cys-Asn-ethanolamine-PO4-6(Man1- 2)Man1-2Man1-6Man1-4GlcNH(2)1-6myo-inositol-1,2-cyclicPO(4), was revealed by amino acid analysis and Dionex exchange chromatography of fragments generated enzymatically or chemically from the neutral glycan core and is in accordance with the known consensus structures of yeast GPI anchors. PIG-P stimulated glucose transport and lipogenesis in normal, desensitized and receptor-depleted isolated rat adipocytes, increased glycerol-3-phosphate acyltransferase activity and translocation of the glucose transporter isoform 4, and inhibited isoproterenol-induced lipolysis and protein kinase A activation in adipocytes. Furthermore, PIG-P was found to stimulate glucose transport in isolated rat cardiomyocytes and glycogenesis and glycogen synthase in isolated rat diaphragms. The concentration-dependent effects of the PIG-P reached 70-90% of the maximal insulin activity with EC50-values of 0.5-5 mu M. Chemical or enzymic cleavages within the glycan or peptide portion of

the PIG-P led to decrease or loss of activity. The data demonstrate that PIG-P exhibits a potent insulin-mimetic activity which covers a broad spectrum of metabolic insulin actions on glucose transport and metabolism.
CC ENDOCRINOLOGY & METABOLISM
STP KeyWords Plus (R): CAMP-BINDING ECTOPROTEIN; HUMAN ERYTHROCYTE ACETYLCHOLINESTERASE; GLUCOSE-TRANSPORT SYSTEM; GLYCOSYL-PHOSPHATIDYLINOSITOL; SACCHAROMYCES-CEREVISIAE; MEMBRANE-PROTEINS; LIPOPROTEIN-LIPASE; LIPOLYTIC CLEAVAGE; SULFONYLUREA DRUG; 3T3 ADIPOCYTES
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L135 ANSWER 28 OF 38 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 1997:821793 SCISEARCH Full-text
GA The Genuine Article (R) Number: YF494
TI Osmotic stress activates phosphatidylinositol-3,5-bisphosphate synthesis
AU Dove S K (Reprint)
CS UNIV BIRMINGHAM, CTR CLIN RES IMMUNOL & SIGNALLING, BIRMINGHAM B15 2TT, W MIDLANDS, ENGLAND (Reprint)
AU Cooke F T; Douglas M R; Sayers L G; Parker P J; Michell R H
CS UNIV BIRMINGHAM, DEPT BIOCHEM, BIRMINGHAM B15 2TT, W MIDLANDS, ENGLAND; UNIV BIRMINGHAM, DEPT RHEUMATOL, BIRMINGHAM B15 2TT, W MIDLANDS, ENGLAND; IMPERIAL CANC RES FUND, LONDON WC2A 3PX, ENGLAND
CYA ENGLAND
SO NATURE, (13 NOV 1997) Vol. 390, No. 6656, pp. 187-192.
ISSN: 0028-0836.
PB MACMILLAN MAGAZINES LTD, PORTERS SOUTH, 4 CRINAN ST, LONDON, ENGLAND N1 9XW.
DT Article; Journal
FS PHYS; LIFE; AGRI
LA English
REC Reference Count: 27
ED Entered STN: 1997
Last Updated on STN: 1997
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
ED Entered STN: 1997
Last Updated on STN: 1997
AB Inositol phospholipids play multiple roles in cell signalling systems. Two widespread eukaryotic phosphoinositide-based signal transduction mechanisms, phosphoinositidase C-catalysed phosphatidylinositol-4,5-bisphosphate (PtdIns(4,5)P-2) hydrolysis and 3-OH kinase-catalysed PtdIns(4,5)P-2 phosphorylation, make the second messengers inositol 1,4,5-trisphosphate (Ins(1,4,5)P-3) sn-1,2-diacylglycerol and PtdIns(3,4,5)P-3 (refs 1-7). In addition, PtdIns(4,5)P-2 and PtdIns3P have been implicated in exocytosis and membrane trafficking(8). We now show that when the yeasts Saccharomyces cerevisiae and Schizosaccharomyces pombe are hyperosmotically stressed, they rapidly synthesize phosphatidylinositol-3,5-bisphosphate (PtdIns(3,5)P-2) by a process that involves activation of a PtdIns3P 5-OH kinase. This PtdIns(3,5)P-2 accumulation only occurs in yeasts that have an active vps34-encoded PtdIns 3-OH kinase, showing that this latter kinase makes the PtdIns3P needed for PtdIns(3,5)P-2 synthesis and indicating that PtdIns(3,5)P-2 may have a role in sorting vesicular proteins. PtdIns(3,5)P-2 is also present in mammalian and plant cells: in monkey Cos-7 cells, its labelling is inversely related to the external osmotic pressure. The stimulation of a PtdIns3P 5-OH kinase-catalysed synthesis of PtdIns(3,5)P-2, a molecule that might be a new type of phosphoinositide 'second messenger', thus appears to be central to a widespread and previously uncharacterized regulatory pathway.
CC MULTIDISCIPLINARY SCIENCES
STP KeyWords Plus (R): INOSITOL PHOSPHATE ISOMERS; LIQUID-

CHROMATOGRAPHY; CELLS; PHOSPHATIDYLINOSITOL(3,4,5)-TRISPHOSPHATE; POLYPHOSPHOINOSITIDE; TRISPHOSPHATE; PURIFICATION; METABOLISM; PATHWAY; YEAST
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L135 ANSWER 29 OF 38 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 1993:535469 SCISEARCH Full-text
GA The Genuine Article (R) Number: LU493
TI GENETIC AND BIOCHEMICAL-CHARACTERIZATION OF A PHOSPHATIDYLINOSITOL -SPECIFIC PHOSPHOLIPASE-C IN SACCHAROMYCES-CEREVISIAE
AU FLICK J S (Reprint); THORNER J
CS UNIV CALIF BERKELEY, DEPT MOLEC & CELL BIOL, DIV BIOCHEM & MOLEC BIOL, BERKELEY, CA 94720
CYA USA
SO MOLECULAR AND CELLULAR BIOLOGY, (SEP 1993) Vol. 13, No. 9, pp. 5861-5876.
ISSN: 0270-7306.
PB AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 75
ED Entered STN: 1994
Last Updated on STN: 1994
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
ED Entered STN: 1994
Last Updated on STN: 1994
AB Hydrolysis of phosphatidylinositol 4,5-bisphosphate (PIP2) by phosphatidylinositol-specific phospholipase C (PI-PLC) generates two second messengers, inositol 1,4,5-trisphosphate and 1,2-diacylglycerol. The polymerase chain reaction was used to isolate a Saccharomyces cerevisiae gene (PLC1) that encodes a protein of 869 amino acids (designated Plc1p) that bears greatest resemblance to the delta isoforms of mammalian PI-PLC in terms of overall sequence similarity and domain arrangement. Plc1p contains the conserved X and Y domains found in all higher eukaryotic PI-PLCs (51 and 29% identity, respectively, to the corresponding domains of rat delta1 PI-PLC) and also contains a presumptive Ca2+-binding site (an E-F hand motif). Plc1p, modified by in-frame insertion of a His, tract and a c-myc epitope near its amino terminus, was overexpressed from the GAL1 promoter, partially purified by nickel chelate affinity chromatography, and shown to be an active PLC enzyme in vitro with properties similar to those of its mammalian counterparts. Plc1p activity was strictly Ca2+ dependent: at a high Ca2+ concentration (0.1 mM), the enzyme hydrolyzed PIP2 at a faster rate than phosphatidylinositol, and at a low Ca2+ concentration (0.5 muM), it hydrolyzed PIP, exclusively. Cells carrying either of two different deletion-insertion mutations (plc1DELTA1::HIS3 and plc1DELTA2::LEU2) were viable but displayed several distinctive phenotypes, including temperature-sensitive growth (inviable above 35-degrees-C), osmotic sensitivity, and defects in the utilization of galactose, raffinose, and glycerol at permissive temperatures (23 to 30-degrees-C). The findings reported here suggest that hydrolysis of PIP2 in S. cerevisiae is required for a number of nutritional and stress-related responses.
CC BIOCHEMISTRY & MOLECULAR BIOLOGY; CELL BIOLOGY
STP KeyWords Plus (R): PROTEIN-KINASE-C; GLUCOSE REPRESSION; SHUTTLE VECTORS; POINT MUTATION; BOVINE BRAIN; CELL-CYCLE; YEAST; DNA; PURIFICATION; SEQUENCES
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L135 ANSWER 30 OF 38 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 1992:715931 SCISEARCH Full-text
GA The Genuine Article (R) Number: KB603
TI THE CAMP-BINDING ECTOPROTEIN FROM SACCHAROMYCES-CEREVISIAE IS MEMBRANE-ANCHORED BY GLYCOSYL-PHOSPHATIDYLINOSITOL
AU MULLER G (Reprint)
CS HOECHST AG, DIV PHARMACEUT RES, SBU METAB H825, POB 800320, W-6230 FRANKFURT 80, GERMANY (Reprint)
AU SCHUBERT K; FIEDLER F; BANDLOW W
CS UNIV MUNICH, INST GENET & MIKROBIOL, W-8000 MUNICH 19, GERMANY
CYA GERMANY
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (15 DEC 1992) Vol. 267, No. 35, pp. 25337-25346.
ISSN: 0021-9258.
PB AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA.
DT Article; Journal
LA English
REC Reference Count: 51
ED Entered STN: 1994
Last Updated on STN: 1994
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
ED Entered STN: 1994
Last Updated on STN: 1994
AB Saccharomyces cerevisiae contains an amphiphilic cAMP-binding glycoprotein at the outer face of the plasma membrane (M(r) = 54,000). It is converted to a hydrophilic form by treatment with glycosyl-phosphatidylinositol-specific phospholipases C and D (GPI-PLC/D), suggesting membrane anchorage by a covalently bound glycolipid. Determination of the constituents of the purified anchor by gas-liquid chromatography and amino acid analysis reveals the presence of glycerol, myo-inositol, glucosamine, galactose, mannose, ethanolamine, and asparagine (as the carboxyl-terminal amino acid of the Pronase-digested protein to which the anchor is attached). Complementary results are obtained by metabolic labeling, indicating that fatty acids and phosphorus are additional anchor constituents. The phosphorus is resistant to alkaline phosphatase, whereas approximately half is lost from the protein after treatment with GPI-PLD or nitrous acid, and all is removed by aqueous HF indicating the presence of two phosphodiester bonds. Inhibition of N-glycosylation by tunicamycin or removal of protein-bound glycan chains by N-glycanase or Pronase does not abolish radiolabeling of the anchor structure by any of the above compounds. Analysis of the products obtained after sequential enzymic and chemical degradation of the anchor agrees with the arrangement of constitutents in GPIs from higher eucaryotes. Evidence for anchorage of the yeast cAMP-binding protein by a GPI anchor is strengthened additionally by the reactivity of the GPI-PLC-cleaved anchor with antibodies directed against the cross-reacting determinant of trypanosomal variant surface glycoproteins.
CC BIOCHEMISTRY & MOLECULAR BIOLOGY
STP KeyWords Plus (R): VARIANT SURFACE GLYCOPROTEIN; TRYPANOSOMA-BRUCEI; YEAST MITOCHONDRIA; PHOSPHOLIPASE-C; SUBMITOCHONDRIAL LOCALIZATION; INTRAMITOCHONDRIAL LOCATION; SYNERGISTIC CONTROL; PLASMA-MEMBRANE; PROTEIN; INSULIN
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L135 ANSWER 31 OF 38 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 1992:692280 SCISEARCH Full-text

GA The Genuine Article (R) Number: JZ239
TI PURIFICATION AND CHARACTERIZATION OF A SOLUBLE PHOSPHATIDYLINOSITOL 4-KINASE FROM THE YEAST SACCHAROMYCES -CEREVISIAE
AU FLANAGAN C A (Reprint); THORNER J
CS UNIV CALIF BERKELEY, DEPT MOLEC & CELL BIOL, DIV BIOCHEM & MOLEC BIOL, RM 401, BARKER HALL, BERKELEY, CA 94720
CYA USA
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (25 NOV 1992) Vol. 267, No. 33, pp. 24117-24125.
ISSN: 0021-9258.
PB AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 60
ED Entered STN: 1994
Last Updated on STN: 1994
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
ED Entered STN: 1994
Last Updated on STN: 1994
AB A phosphatidylinositol (PI) 4-kinase was purified 25,000-fold from the cytosolic fraction of extracts from the yeast Saccharomyces cerevisiae. The purification consisted of an ammonium sulfate fractionation followed by chromatography on sulfonated-agarose (S-Sepharose), phosphocellulose, threonine-agarose, and quaternary amino (Mono Q), and sulfonated (Mono S) beads. Major contaminants in the purification, Hsc82 and Hsp82 (yeast homologs of the mammalian heat shock protein Hsp90), were eliminated by using a combination of molecular genetics (to construct a null mutation in HSC82), altered growth conditions (to minimize expression from the inducible HSP82 gene), and high ionic strength fractionation conditions (to remove the residual Hsp82). The purified enzyme had an apparent subunit molecular weight of 125,000, much larger than any other well characterized PI-4-kinase reported previously. Like mammalian PI-4-kinases, the yeast enzyme specifically phosphorylated PI on position 4 of the inositol ring and was stimulated by Triton X-100. However, activity was not inhibited by adenosine, a potent inhibitor of certain (type II) mammalian PI-4-kinases. The enzyme displayed typical Michaelis-Menten kinetics with apparent K(m) values of 100 muM for ATP and 50 muM for PI. To date, this yeast enzyme is the first soluble PI-4-kinase purified from any source.
CC BIOCHEMISTRY & MOLECULAR BIOLOGY
STP KeyWords Plus (R): PROTEIN-KINASE-C; PHOSPHOLIPASE-C; BOVINE BRAIN; SIGNAL TRANSDUCTION; TYROSINE PHOSPHORYLATION; INOSITOL TRISPHOSPHATE; 2ND MESSENGERS; RAT-LIVER; GENE; RECEPTOR
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L135 ANSWER 32 OF 38 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 1992:494208 SCISEARCH Full-text
GA The Genuine Article (R) Number: JJ458
TI PURIFICATION, CHARACTERIZATION, AND KINETIC-ANALYSIS OF A 55-KDA FORM OF PHOSPHATIDYLINOSITOL 4-KINASE FROM SACCHAROMYCES-CEREVISIAE
AU NICKELS J T (Reprint); BUXEDA R J; CARMAN G M
CS RUTGERS STATE UNIV, COOK COLL, NEW JERSEY AGR EXPT STN, DEPT FOOD SCI, NEW BRUNSWICK, NJ 08903
CYA USA
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (15 AUG 1992) Vol. 267, No. 23, pp. 16297-16304.

ISSN: 0021-9258.
PB AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 52
ED Entered STN: 1994
Last Updated on STN: 1994
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
ED Entered STN: 1994
Last Updated on STN: 1994
AB A 55-kDa form of membrane-associated phosphatidylinositol 4-kinase (ATP:phosphatidylinositol 4-phosphotransferase, EC 2.7.1.67) was purified 10,166-fold from Saccharomyces cerevisiae. The purification procedure included solubilization of microsome membranes with 1% Triton X-100 followed by chromatography with DE52, hydroxylapatite I, Q-Sepharose, Mono Q, and hydroxylapatite II. The procedure resulted in a nearly homogeneous 55-kDa phosphatidylinositol 4-kinase preparation. The 55-kDa phosphatidylinositol 4-kinase and the previously purified 45-kDa phosphatidylinositol 4-kinase differed with respect to their amino acid composition, isoelectric points, and peptide maps. Furthermore, the two forms of phosphatidylinositol 4-kinase did not show an immunological relationship. Maximum 55-kDa phosphatidylinositol 4-kinase activity was dependent on magnesium (10 mM) or manganese (0.5 mM) ions and Triton X-100 at the pH optimum of 7.0. The activation energy for the reaction was 12 kcal/mol, and the enzyme was labile above 30-degrees-C. The enzyme was inhibited by thioreactive agents, MgADP, and calcium ions. A detailed kinetic analysis of the purified enzyme was performed using Triton X-100/phosphatidylinositol-mixed micelles. 55-kDa phosphatidylinositol 4-kinase activity followed saturation kinetics with respect to the bulk and surface concentrations of phosphatidylinositol and followed surface dilution kinetics. The interfacial Michaelis constant (K(m)) and the dissociation constant (K(s)) for phosphatidylinositol in the Triton X-100 micelle surface were 1.3 mol % and 0.035 mM, respectively. The K(m) for MgATP was 0.36 mM. 55-kDa phosphatidylinositol 4-kinase catalyzed a sequential reaction mechanism as indicated by the results of kinetic and isotopic exchange reactions. The enzyme bound to phosphatidylinositol before ATP and released phosphatidylinositol 4-phosphate before ADP. The enzymological and kinetic properties of the 55-kDa phosphatidylinositol 4-kinase differed significantly from those of the 45-kDa phosphatidylinositol 4-kinase. This may suggest that the two forms of phosphatidylinositol 4-kinase from S. cerevisiae are regulated differentially in vivo.
CC BIOCHEMISTRY & MOLECULAR BIOLOGY
STP KeyWords Plus (R): SODIUM DODECYL-SULFATE; MIXED MICELLES; GEL-ELECTROPHORESIS; CELL-PROLIFERATION; TRITON X-100; PHOSPHATIDATE PHOSPHATASE; MEMBRANE-PROTEINS; ESCHERICHIA-COLI; KINASE; PHOSPHOLIPASE-A2
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L135 ANSWER 33 OF 38 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 1992:438975 SCISEARCH Full-text
GA The Genuine Article (R) Number: JE019
TI PURIFICATION OF A PHOSPHATIDYLINOSITOL PHOSPHATIDYLCHOLINE TRANSFER PROTEIN FROM NEUROSPORA-CRASSA
AU BASU J (Reprint); KUNDU M; CHAKRABARTI P
CS BOSE INST, DEPT CHEM, 93-1 APC RD, CALCUTTA 700009, W BENGAL, INDIA
CYA INDIA
SO BIOCHIMICA ET BIOPHYSICA ACTA, (26 JUN 1992) Vol. 1126, No. 3, pp. 286-290.

ISSN: 0006-3002.
PB ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 17
ED Entered STN: 1994
Last Updated on STN: 1994
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
ED Entered STN: 1994
Last Updated on STN: 1994
AB This paper reports, for the first time, the purification of a phospholipid transfer protein (PLTP) from a fungus, Neurospora crassa. The protein was purified from the post-microsomal supernatant of N. crassa by successive chromatography on DEAE-cellulose, Sephadex-G75 and PBE 94 (pH 4-7). The purified protein (M(r) 38 000) was found to transfer phosphatidylinositol preferentially over phosphatidylcholine, like the PLTP from the yeast, Saccharomyces cerevisiae. PC transfer was completely inhibited by inactivation of free amino groups or tryptophan residues. Surprisingly, the protein did not cross-react with antibodies against the bovine brain PITP. The cellular content of the protein was maximal during the logarithmic phase of growth. However, no direct correlation between the content of the protein and PC transfer activity could be demonstrated.
CC BIOPHYSICS; BIOCHEMISTRY & MOLECULAR BIOLOGY
ST Author Keywords: PHOSPHOLIPID TRANSFER PROTEIN; PROTEIN PURIFICATION; (NEUROSPORA-CRASSA)
STP KeyWords Plus (R): PHOSPHOLIPID TRANSFER PROTEINS; YEAST GOLGI; SACCHAROMYCES-CEREVISIAE; BOVINE LIVER
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L135 ANSWER 34 OF 38 DISSABS COPYRIGHT (C) 2009 ProQuest Information and Learning Company; All Rights Reserved on STN
AN 1999:25478 DISSABS Order Number: AAI9912214
TI BIOSYNTHESIS AND CHARACTERIZATION OF EARLY GLYCOSYLPHOSPHATIDYLINOSITOL ANCHOR INTERMEDIATES IN SACCHAROMYCES CEREVISIAE
AU COSTELLO, LISA CATHERINE [PH.D.]; ORLEAN, PETER A. B. [adviser]
CS UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN (0090)
SO Dissertation Abstracts International, (1998) Vol. 59, No. 11B, p. 5831. Order No.: AAI9912214. 125 pages.
DT Dissertation
FS DAI
LA English
AB A glycosylphosphatidylinositol (GPI) anchor is a lipid modification of protein that serves to attach a protein to the outer surface of the plasma membrane or to the lumenal face of a secretory vesicle. My research focused on developing S. cerevisiae as a model system to study GPI anchor biosynthesis. I wished to elucidate the steps involved in early GPI anchor assembly and to characterize the intermediates made in these steps.
I found that S.cerevisiae did have GPI biosynthetic activities and developed in vitro assays to detect the synthesis of the first three GPI biosynthetic intermediates. By chemical and enzymatic methods, I characterized these intermediates as GIcNAc-PI, GIcNH2-Pl, and GIcNH2(acyl-inositol)-PI. The origin of the acyl group esterified to the inositol, which renders the GPI molecule resistant to cleavage by phosphatidylinositol specific-phospholipase C (PI-PLC), was then explored in depth. I found that inositol acylation in yeast was acyl-CoA-dependent, a novel reaction in GPI anchor biosynthesis. Furthermore, I have developed a yeast crude lysate assay which detects the synthesis

of putative mannosylated GPI anchor intermediates. Next, it was desired to obtain structural information on in vivo GPI anchor intermediates. To address this issue, I exploited the fact that at non-permissive temperature, the yeast dpm1-6 mutant accumulates GlcNH2-(acyl-inositol)-PI. This precursor molecule is the earliest biosynthetic intermediate that can be detected in in vivo radiolabeling experiments. I isolated this lipid and had it analyzed by liquid chromatography - mass spectroscopy (LC-MS) with an electrospray interface. The results show that this intermediate has very long chain fatty acids, most likely on its diacylglycerol moiety. This has significant implications for GPI anchor biosynthesis in yeast and suggests that GPI anchors are either assembled on a specialized PI or that the diacylglycerol moiety on early GPI precursor molecules are rapidly remodeled.

CC 0487 CHEMISTRY, BIOCHEMISTRY; 0307 BIOLOGY, MOLECULAR

L135 ANSWER 35 OF 38 DISSABS COPYRIGHT (C) 2009 ProQuest Information and Learning Company; All Rights Reserved on STN

AN 97:16017 DISSABS Order Number: AARC537923 (not available for sale by UMI)

TI CHARACTERIZATION OF MEMBRANE-ASSOCIATED LIPID TRANSFER PROTEINS OF THE YEAST SACCHAROMYCES CEREVISIAE (PHOSPHATIDYLINOSITOL, PHOSPHATIDYLCHOLINE)
CHARAKTERISIERUNG MEMBRANASSOZIIERTER: LIPID-TRANSFERPROTEINE IN DER HEFE SACCHAROMYCES CEREVISIAE

AU CEOLOTTO, CHRISTIAN [DR.]

CS TECHNISCHE UNIVERSITAET GRAZ (AUSTRIA) (5800)

SO Dissertation Abstracts International, (1996) Vol. 58, No. 1C, p. 82. Order No.: AARC537923 (not available for sale by UMI). 137 pages. TECHNISCHE UNIVERSITAT GRAZ, AUSSENINSTITUT, GRAZ, AUSTRIA.

DT Dissertation

FS DAI

LA German

ED Entered STN: 19970305
Last Updated on STN: 19970305

ED Entered STN: 19970305
Last Updated on STN: 19970305

AB Lipid transfer proteins isolated from various types of cells can be grouped into three categories, namely phosphatidylinositol transfer proteins, phosphatidylcholine transfer proteins and the so-called non-specific lipid transfer protein. Two types of phospholipid transfer proteins have been isolated from the cytosol of the yeast Saccharomyces cerevisiae. The yeast phosphatidylinositol transfer protein which resembles mammalian phosphatidylinositol transfer proteins, and phosphatidylserine transfer protein which resembles the mammalian non-specific lipid transfer protein regarding the broad substrate specificity. Recently membrane-bound forms of lipid transfer proteins were discovered in the yeast Saccharomyces cerevisiae. A lipid transfer protein with a broad substrate specificity is associated with yeast peroxisomal membranes. This protein catalyzes in vitro the transfer of various phospholipids, phosphatidylinositol, and phosphatidylserine being translocated at the highest rates. The transfer protein is released from peroxisomal membranes by treatment with 0.25 M KCl. Using conventional chromatographic techniques the protein was 1860-fold enriched over the homogenate. It is inactivated by heat, detergents, divalent cations and proteases. During various steps of purification the lipid transfer protein co-fractionated with peroxisomal acyl-CoA oxidase. In a pox1 mutant strain which lacks acyl-CoA oxidase peroxisomal lipid transfer activity was still present, although at a slightly reduced rate. The peroxisomal lipid transfer protein from the mutant exhibited different chromatographic properties as compared to

that of the wild-type strain. These data suggest that acyl-CoA oxidase and the peroxisomal lipid transfer protein may form a complex. Another representative of membrane-bound lipid transfer proteins was enriched from mitochondria and characterized. Its substrate specificity is similar to the cytosolic PSTP and the peroxisomal lipid transfer protein. Similar to the peroxisomal protein, but in contrast to the cytosolic lipid transfer proteins the mitochondrial form has a molecular weight of about 70,000 kDa.

CC 0379 BIOLOGY, CELL; 0487 CHEMISTRY, BIOCHEMISTRY

L135 ANSWER 36 OF 38 DISSABS COPYRIGHT (C) 2009 ProQuest Information and Learning Company; All Rights Reserved on STN

AN 94:17275 DISSABS Order Number: AAR9412897

TI PURIFICATION AND CHARACTERIZATION OF 45-KDA AND 55-KDA FORMS OF PHOSPHATIDYLINOSITOL 4-KINASE FROM SACCHAROMYCES CEREVISIAE

AU NICKELS, JOSEPH THOMAS, JR. [PH.D.]; CARMAN, GEORGE M. [advisor]

CS RUTGERS THE STATE U. OF N.J. - NEW BRUNSWICK AND U.M.D.N.J. (0801)

SO Dissertation Abstracts International, (1993) Vol. 54, No. 11B, p. 5517. Order No.: AAR9412897. 119 pages.

DT Dissertation

FS DAI

LA English

ED Entered STN: 19940426
Last Updated on STN: 19940426

ED Entered STN: 19940426
Last Updated on STN: 19940426

AB Two membrane-associated forms (45-kDa and 55-kDa) of phosphatidylinositol (PI) 4-kinase (ATP:phosphatidylinositol 4-phosphotransferase, EC 2.7.1.67) were purified and characterized from the yeast Saccharomyces cerevisiae. The 45-kDa PI 4-kinase was purified by an improved procedure over that previously reported for a 35-kDa form of the enzyme. The 35-kDa enzyme was a proteolytic product of the 45-kDa PI 4-kinase. 55-kDa PI 4-kinase was purified 10,166-fold by a procedure which included the solubilization of microsome membranes with 1% Triton X-100 followed by chromatography with DE-52, hydroxylapatite I, Q-Sepharose, Mono Q, and hydroxylapatite II. The 45- and 55-kDa forms of PI 4-kinase differed with respect to their amino acid compositions, isoelectric points, and peptide maps. Furthermore, the two forms of the enzyme did not show an immunological relationship. Maximum 55-kDa PI 4-kinase activity was dependent on magnesium (10 mM) or manganese (0.5 mM) ions and Triton X-100 at the pH optimum of 7.0. The activation energy for the reaction was 12 kcal/mol, and the enzyme was labile above 30$\sp\circ$C. The enzyme was inhibited by thioreactive agents, MgADP, and calcium ions. Previous studies using crude preparations of PI 4-kinase suggested that the enzyme is regulated by the RAS/cAMP pathway and/or ATP and ADP levels. Purified 45- and 55-kDa PI 4-kinases were neither phosphorylated nor regulated by cAMP-dependent protein kinase. Work from our laboratory has shown that 45- and 55-kDa PI 4-kinase activities are regulated by ADP by a competitive mechanism with respect to ATP. Azidonucleotide photoaffinity labeling probes were used to define the ATP and ADP sites on the PI 4-kinases. The photoprobes 8-azidoATP and 8-azidoADP fulfilled the criteria of specific photoaffinity labels for both PI 4-kinases. 8 azidoATP and 8-azidoADP were competitive inhibitors of the PI 4-kinases with $K\sb{i}$ values similar to the $K\sb{m}$ for ATP. Both photoprobes photoinactivated the enzymes in a dose-dependent manner. ATP, the true substrate, provided specific protection against photoinactivation, whereas GTP, a nonspecific nucleotide, provided no protection from photoinactivation. Photoaffinity labeling of the PI 4-kinases with 8-azidoATP was specifically prevented

with both ATP and ADP. These data support the conclusion that the ATP and ADP sites of the 45- and 55-kDa PI 4-kinases were the same.
CC 0410 BIOLOGY, MICROBIOLOGY

L135 ANSWER 37 OF 38 DISSABS COPYRIGHT (C) 2009 ProQuest Information and Learning Company; All Rights Reserved on STN
AN 89:26309 DISSABS Order Number: AAR9008881
TI PURIFICATION AND CHARACTERIZATION OF PHOSPHATIDYLINOSITOL KINASE FROM SACCHAROMYCES CEREVISIAE
AU BELUNIS, CHARLES JOHN [PH.D.]; CARMAN, GEORGE M. [advisor]
CS RUTGERS THE STATE UNIVERSITY OF NEW JERSEY - NEW BRUNSWICK (0190)
SO Dissertation Abstracts International, (1989) Vol. 50, No. 11B, p. 5028. Order No.: AAR9008881. 105 pages.
DT Dissertation
FS DAI
LA English
ED Entered STN: 19921118
Last Updated on STN: 19921118
ED Entered STN: 19921118
Last Updated on STN: 19921118
AB The membrane-associated phospholipid biosynthetic enzyme phosphatidylinositol kinase (ATP:phosphatidylinositol 4-phosphotransferase EC 2.7.1.67) was purified 8,000-fold from Saccharomyces cerevisiae. The purification procedure included Triton X-100 solubilization of microsomal membranes, DE-52 chromatography, hydroxylapatite chromatography, octyl Sepharose chromatography, and two consecutive Mono Q chromatographic steps. The procedure resulted in the isolation of a protein with a subunit molecular weight of 35,000 that was 96% of homogeneity as evidenced by native and SDS-polyacrylamide gel electrophoresis. Phosphatidylinositol kinase activity was associated with the purified $M\sb{\rm r}$-30,000 subunit. Maximum phosphatidylinositol kinase activity was dependent on magnesium ions and Triton X-100 at pH 8. The true $K\sb{\rm m}$ values for phosphatidylinositol and ATP were 70 μM and 0.3 mM, and the true $V\sb{\rm max}$ was 4750 nmol/min/mg. The turnover number for the enzyme was 142 min$\sp{-1}$. Results of kinetic and isotopic exchange reactions indicated that phosphatidylinositol kinase catalyzed a sequential Bi Bi reaction mechanism. The enzyme bound to phosphatidylinositol prior to ATP and phosphatidylinositol 4-phosphate was the first product released in the reaction. The equilibrium constant for the reaction indicated that the reverse reaction was favored in vitro. The activation energy for the reaction was 31.5 kcal/mol, and the enzyme was thermally labile above 30$\sp\circ$C. Phosphatidylinositol kinase activity was inhibited by calcium ions and thioreactive agents. Various nucleotides including adenosine and S-adenosylhomocysteine did not affect phosphatidylinositol kinase activity. cAMP-dependent protein kinase catalyzed the phosphorylation of the phosphatidylinositol kinase $M\sb{\rm r}$-35,000 subunit which resulted in a reduction of phosphatidylinositol kinase activity.
CC 0487 CHEMISTRY, BIOCHEMISTRY

L135 ANSWER 38 OF 38 DISSABS COPYRIGHT (C) 2009 ProQuest Information and Learning Company; All Rights Reserved on STN
AN 86:4396 DISSABS Order Number: AAR8612116
TI RECONSTITUTION OF PURIFIED PHOSPHATIDYLINOSITOL SYNTHASE FROM SACCHAROMYCES CEREVISIAE INTO PHOSPHOLIPID VESICLES
AU FISCHL, ANTHONY STEPHEN [PH.D.]
CS RUTGERS THE STATE UNIVERSITY OF NEW JERSEY - NEW BRUNSWICK (0190)
SO Dissertation Abstracts International, (1986) Vol. 47, No. 3B, p. 855. Order No.: AAR8612116. 138 pages.

DT Dissertation
FS DAI
LA English
ED Entered STN: 19921118
Last Updated on STN: 19921118
ED Entered STN: 19921118
Last Updated on STN: 19921118
AB Membrane-associated phosphatidylinositol synthase (CDP-diacylglycerol:myo-inositol 3-phosphatidyltransferase, EC 2.7.8.11) from Saccharomyces cerevisiae was purified (Fischl, A.S., and Carman, G.M. 1983 J. Bacteriol. 154, 304-311) and reconstituted into unilamellar phospholipid vesicles. The enzyme was reconstituted into vesicles by removing detergent from an octylglucoside-phospho- lipid-Triton X-100-enzyme mixed micelle mixture by Sephadex G-50 superfine column chromatography. The average diameter of the vesicles was 40 nm and chymotrypsin treatment of intact vesicles indicated that over 90% of the reconstituted enzyme had its active site facing outward. The enzymological properties of reconstituted phosphatidylinositol synthase were determined in the absence of detergent. Reconstituted PI synthase was studied in a variety of phospholipid vesicles. Maximum phosphatidylinositol synthase activity was found when the enzyme was reconstituted into phos-phatidylcholine:phosphatidylethanolamine:phosphatidylinositol: phosphatidylserine vesicles. Phosphatidylserine stimulated reconstituted enzyme activity. The reconstituted enzyme was not effected by water-soluble phospholipid precursors or nucleotides.
CC 0473 AGRICULTURE, GENERAL

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L3              QUE  SPE=ON  ABB=ON  PLU=ON  G01N0033/IPC
L6              QUE  SPE=ON  ABB=ON  PLU=ON  TSUKAHARA, K?/AU,AUTH
L7              QUE  SPE=ON  ABB=ON  PLU=ON  TSUCHIYA, M?/AU,AUTH
L8              QUE  SPE=ON  ABB=ON  PLU=ON  JIGAMI, Y?/AU,AUTH
L9              QUE  SPE=ON  ABB=ON  PLU=ON  NAKAYAMA, K?/AU,AUTH
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L12             QUE  SPE=ON  ABB=ON  PLU=ON  EISAI/CS,SO,PA OR ((NATIONAL
                 (1W)(INST OR INSTITUTE))(5A)(ADVANCED(1W)INDUSTRIAL)(5A)
                (SCIENCE (3W)(TECH OR TECHNOL OR TECHNOLOGY)))/CS,SO,PA
L13             QUE  SPE=ON  ABB=ON  PLU=ON  ANTAGON? OR INHIBIT? OR PROH
                IBIT? OR PREVENT? OR DIMINISH? OR REDUC? OR IMPED? OR DEP
                RESS? OR SUPPRESS? OR REPRESS? OR OBSTRUCT? OR RESTRICT?
                OR TERMINAT? OR BLOCK? OR STOP? OR RETARD? OR SLOW? OR DE
                LAY? OR LIMIT? OR DECREAS? OR LOWER? OR LESSEN? OR MINIMI
                Z? OR MINIMIS? OR DISRUPT?
L14             QUE  SPE=ON  ABB=ON  PLU=ON  FUNGUS OR FUNGI OR FUNGAL?
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                NGISTAT?
L16             QUE  SPE=ON  ABB=ON  PLU=ON  SCREEN? OR TEST OR TESTING O
                R TESTED OR EVALUAT? OR DETERMIN?
L17             QUE  SPE=ON  ABB=ON  PLU=ON  OVEREXPRESS? OR (OVER(1W)EXP
                RESS?)
L18             QUE  SPE=ON  ABB=ON  PLU=ON  PROTEIN
L19             QUE  SPE=ON  ABB=ON  PLU=ON  GWT1 OR (GWT(1W)(1 OR I)) OR
                 GWTI
L20             QUE  SPE=ON  ABB=ON  PLU=ON  GENE
L21             QUE  SPE=ON  ABB=ON  PLU=ON  SACCHAROMYC? OR CEREVIS?
L22             QUE  SPE=ON  ABB=ON  PLU=ON  TEST OR TESTING OR TESTED OR
                 DETECT? OR DETERMIN? OR ANALY? OR SENSE OR SENSED OR SEN
                SING OR BIOSENS? OR ?ASSAY? OR ?MEASUR?
L23             QUE  SPE=ON  ABB=ON  PLU=ON  ANCHOR?
L24             QUE  SPE=ON  ABB=ON  PLU=ON  GPI
L25             QUE  SPE=ON  ABB=ON  PLU=ON  PI
L26             QUE  SPE=ON  ABB=ON  PLU=ON  ?GLYCOS? OR GLC?
L27             QUE  SPE=ON  ABB=ON  PLU=ON  ?PHOSPHATID?
L28             QUE  SPE=ON  ABB=ON  PLU=ON  ?INOSIT?
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                OR (?PHOSPHATID? (1W)?INOSIT?)
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L31             QUE  SPE=ON  ABB=ON  PLU=ON  ACYLAT?
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L33             QUE  SPE=ON  ABB=ON  PLU=ON  CHROMATOG?
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L36             QUE  SPE=ON  ABB=ON  PLU=ON  PROTEINS+PFT,OLD,NEW/CT
L37             QUE  SPE=ON  ABB=ON  PLU=ON  "GENE EXPRESSION"+PFT,OLD,NE
                W,NT/CT
L38             QUE  SPE=ON  ABB=ON  PLU=ON  "DRUG SCREENING"+PFT,OLD,NEW
                ,NT/CT
L39             QUE  SPE=ON  ABB=ON  PLU=ON  FUNGI+PFT,OLD,NEW/CT
L40             QUE  SPE=ON  ABB=ON  PLU=ON  FUNGICIDES+PFT,OLD,NEW/CT
L41             QUE  SPE=ON  ABB=ON  PLU=ON  GLYCOPHOSPHOLIPIDS+PFT,OLD,N
                EW/CT
L42             QUE  SPE=ON  ABB=ON  PLU=ON  ACYLATION+PFT,OLD,NEW/CT
L43          41 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  (GWT1/CNS OR
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L44           6 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  L43
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L46           4 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  (L44 OR L45) (L)(L16
                (L) L13)
L47          21 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  (L44 OR L45) (L)L13
L48          37 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  L45 AND (L19 OR L21)
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                OR (L39 OR L40) OR L38 OR L16 OR L22)
L51           1 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  L50 AND (L33 OR L34)
L52          56 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  (L49 OR L50)
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L54           1 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  L52 AND (L53 OR (L33
                OR L34))
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L56          12 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  L55 AND ((L14 OR L15)
                OR (L39 OR L40))
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L58           4 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  L3 AND L57
L59          12 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  (L57 OR L58)
L60          12 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  L59 AND ((L13 OR L14
                OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23
                OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32
                OR L33 OR L34 OR L35) OR (L36 OR L37 OR L38 OR L39 OR L40 OR
                L41 OR L42))
L61          12 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  (L59 OR L60)
L62           5 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  L61 AND (L6 OR L7 OR
                L8 OR L9 OR L10 OR L11 OR L12)


=> d que l78
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L7              QUE  SPE=ON  ABB=ON  PLU=ON  TSUCHIYA, M?/AU,AUTH
L8              QUE  SPE=ON  ABB=ON  PLU=ON  JIGAMI, Y?/AU,AUTH
L9              QUE  SPE=ON  ABB=ON  PLU=ON  NAKAYAMA, K?/AU,AUTH
L10             QUE  SPE=ON  ABB=ON  PLU=ON  UMEMURA, M?/AU,AUTH
L11             QUE  SPE=ON  ABB=ON  PLU=ON  OKAMOTO, M?/AU,AUTH
L12             QUE  SPE=ON  ABB=ON  PLU=ON  EISAI/CS,SO,PA OR ((NATIONAL
                 (1W)(INST OR INSTITUTE))(5A)(ADVANCED(1W)INDUSTRIAL)(5A)
                (SCIENCE (3W)(TECH OR TECHNOL OR TECHNOLOGY)))/CS,SO,PA
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                RESS? OR SUPPRESS? OR REPRESS? OR OBSTRUCT? OR RESTRICT?
                OR TERMINAT? OR BLOCK? OR STOP? OR RETARD? OR SLOW? OR DE
                LAY? OR LIMIT? OR DECREAS? OR LOWER? OR LESSEN? OR MINIMI
                Z? OR MINIMIS? OR DISRUPT?
L14             QUE  SPE=ON  ABB=ON  PLU=ON  FUNGUS OR FUNGI OR FUNGAL?
L15             QUE  SPE=ON  ABB=ON  PLU=ON  ANTIFUNG? OR FUNGICID? OR FU
                NGISTAT?
L16             QUE  SPE=ON  ABB=ON  PLU=ON  SCREEN? OR TEST OR TESTING O
                R TESTED OR EVALUAT? OR DETERMIN?
L17             QUE  SPE=ON  ABB=ON  PLU=ON  OVEREXPRESS? OR (OVER(1W)EXP
                RESS?)
L18             QUE  SPE=ON  ABB=ON  PLU=ON  PROTEIN
L19             QUE  SPE=ON  ABB=ON  PLU=ON  GWT1 OR (GWT(1W)(1 OR I)) OR
                 GWTI
L20             QUE  SPE=ON  ABB=ON  PLU=ON  GENE
L21             QUE  SPE=ON  ABB=ON  PLU=ON  SACCHAROMYC? OR CEREVIS?
L22             QUE  SPE=ON  ABB=ON  PLU=ON  TEST OR TESTING OR TESTED OR
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                DETECT? OR DETERMIN? OR ANALY? OR SENSE OR SENSED OR SEN
               SING OR BIOSENS? OR ?ASSAY? OR ?MEASUR?
L23            QUE  SPE=ON  ABB=ON  PLU=ON  ANCHOR?
L24            QUE  SPE=ON  ABB=ON  PLU=ON  GPI
L25            QUE  SPE=ON  ABB=ON  PLU=ON  PI
L26            QUE  SPE=ON  ABB=ON  PLU=ON  ?GLYCOS? OR GLC?
L27            QUE  SPE=ON  ABB=ON  PLU=ON  ?PHOSPHATID?
L28            QUE  SPE=ON  ABB=ON  PLU=ON  ?INOSIT?
L29            QUE  SPE=ON  ABB=ON  PLU=ON  (?PHOSPHATID? (1T)?INOSIT?)
               OR (?PHOSPHATID? (1W)?INOSIT?)
L30            QUE  SPE=ON  ABB=ON  PLU=ON  N(1W)ACYL?
L31            QUE  SPE=ON  ABB=ON  PLU=ON  ACYLAT?
L32            QUE  SPE=ON  ABB=ON  PLU=ON  THIN(1W)LAYER
L33            QUE  SPE=ON  ABB=ON  PLU=ON  CHROMATOG?
L34            QUE  SPE=ON  ABB=ON  PLU=ON  TLC
L35            QUE  SPE=ON  ABB=ON  PLU=ON  CELL(2A)(WALL OR SURFACE)
L68         2681 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L13 (7A)(L19 OR (L24 OR
               L25) OR L29)
L69          209 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L68 AND L3
L70          418 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L68 (15A)(L16 OR L22)
L71          552 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  (L69 OR L70)
L72           10 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L71 AND (L19 OR L21)
L73          102 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L68 AND ((L13(5A)L24) OR
               L15)
L74            7 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L73 AND  (L19 OR L21)
L75           12 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L72 OR L74
L76           12 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L75 AND (L13 OR L14 OR
               L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR
               L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR
               L33 OR L34 OR L35)
L77           12 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  (L75 OR L76)
L78            6 SEA FILE=WPIX SPE=ON  ABB=ON  PLU=ON  L77 AND (L6 OR L7 OR L8
               OR L9 OR L10 OR L11 OR L12)


=> d que l96
L6             QUE  SPE=ON  ABB=ON  PLU=ON  TSUKAHARA, K?/AU,AUTH
L7             QUE  SPE=ON  ABB=ON  PLU=ON  TSUCHIYA, M?/AU,AUTH
L8             QUE  SPE=ON  ABB=ON  PLU=ON  JIGAMI, Y?/AU,AUTH
L9             QUE  SPE=ON  ABB=ON  PLU=ON  NAKAYAMA, K?/AU,AUTH
L10            QUE  SPE=ON  ABB=ON  PLU=ON  UMEMURA, M?/AU,AUTH
L11            QUE  SPE=ON  ABB=ON  PLU=ON  OKAMOTO, M?/AU,AUTH
L12            QUE  SPE=ON  ABB=ON  PLU=ON  EISAI/CS,SO,PA OR ((NATIONAL
                (1W)(INST OR INSTITUTE))(5A)(ADVANCED(1W)INDUSTRIAL)(5A)
               (SCIENCE (3W)(TECH OR TECHNOL OR TECHNOLOGY)))/CS,SO,PA
L14            QUE  SPE=ON  ABB=ON  PLU=ON  FUNGUS OR FUNGI OR FUNGAL?
L15            QUE  SPE=ON  ABB=ON  PLU=ON  ANTIFUNG? OR FUNGICID? OR FU
               NGISTAT?
L16            QUE  SPE=ON  ABB=ON  PLU=ON  SCREEN? OR TEST OR TESTING O
               R TESTED OR EVALUAT? OR DETERMIN?
L19            QUE  SPE=ON  ABB=ON  PLU=ON  GWT1 OR (GWT(1W)(1 OR I)) OR
                GWTI
L21            QUE  SPE=ON  ABB=ON  PLU=ON  SACCHAROMYC? OR CEREVIS?
L22            QUE  SPE=ON  ABB=ON  PLU=ON  TEST OR TESTING OR TESTED OR
                DETECT? OR DETERMIN? OR ANALY? OR SENSE OR SENSED OR SEN
               SING OR BIOSENS? OR ?ASSAY? OR ?MEASUR?
L24            QUE  SPE=ON  ABB=ON  PLU=ON  GPI
L25            QUE  SPE=ON  ABB=ON  PLU=ON  PI
L29            QUE  SPE=ON  ABB=ON  PLU=ON  (?PHOSPHATID? (1T)?INOSIT?)
               OR (?PHOSPHATID? (1W)?INOSIT?)
```

```
L30             QUE  SPE=ON  ABB=ON  PLU=ON  N(1W)ACYL?
L31             QUE  SPE=ON  ABB=ON  PLU=ON  ACYLAT?
L33             QUE  SPE=ON  ABB=ON  PLU=ON  CHROMATOG?
L34             QUE  SPE=ON  ABB=ON  PLU=ON  TLC
L35             QUE  SPE=ON  ABB=ON  PLU=ON  CELL(2A)(WALL OR SURFACE)
L43          41 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  (GWT1/CNS OR
                (GWT/CNS(1W)(1/CNS OR I/CNS)) OR GWTI/CNS)
L81           0 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L43
L82             QUE  SPE=ON  ABB=ON  PLU=ON  "SACCHAROMYCES CEREVISIAE PR
                OTEINS"+PFT,OLD,NEW,NT/CT
L83        1958 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  (L82 OR L21) AND (L19
                OR (L24 OR L25) OR L29)
L84             QUE  SPE=ON  ABB=ON  PLU=ON  "ANTIFUNGAL AGENTS"+PFT,OLD,
                NEW/CT
L85             QUE  SPE=ON  ABB=ON  PLU=ON  "DRUG EVALUATION, PRECLINICA
                L"+PFT,OLD,NEW,NT/CT
L86        1958 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L81 OR L83
L87          14 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L86 AND (L82(L)AN/CT)

L88        1386 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L86 AND (L84 OR L85
                OR L16 OR L22 OR L33 OR L35 OR (L30 OR L31))
L89          11 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L88 AND L85
L90         591 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L88 AND (L84 OR (L14
                OR L15))
L91         524 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L90 AND (L85 OR L16
                OR L22 OR (L33 OR L34))
L92           5 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L91 AND (L30 OR L31)
L93         122 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L91 AND L35
L94          30 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L87 OR L89 OR L92
L95           6 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L93 AND L94
L96           1 SEA FILE=MEDLINE SPE=ON  ABB=ON  PLU=ON  L95 AND (L6 OR L7 OR
                L8 OR L9 OR L10 OR L11 OR L12)


=> d que l112
L6              QUE  SPE=ON  ABB=ON  PLU=ON  TSUKAHARA, K?/AU,AUTH
L7              QUE  SPE=ON  ABB=ON  PLU=ON  TSUCHIYA, M?/AU,AUTH
L8              QUE  SPE=ON  ABB=ON  PLU=ON  JIGAMI, Y?/AU,AUTH
L9              QUE  SPE=ON  ABB=ON  PLU=ON  NAKAYAMA, K?/AU,AUTH
L10             QUE  SPE=ON  ABB=ON  PLU=ON  UMEMURA, M?/AU,AUTH
L11             QUE  SPE=ON  ABB=ON  PLU=ON  OKAMOTO, M?/AU,AUTH
L12             QUE  SPE=ON  ABB=ON  PLU=ON  EISAI/CS,SO,PA OR ((NATIONAL
                 (1W)(INST OR INSTITUTE))(5A)(ADVANCED(1W)INDUSTRIAL)(5A)
                (SCIENCE (3W)(TECH OR TECHNOL OR TECHNOLOGY)))/CS,SO,PA
L13             QUE  SPE=ON  ABB=ON  PLU=ON  ANTAGON? OR INHIBIT? OR PROH
                IBIT? OR PREVENT? OR DIMINISH? OR REDUC? OR IMPED? OR DEP
                RESS? OR SUPPRESS? OR REPRESS? OR OBSTRUCT? OR RESTRICT?
                OR TERMINAT? OR BLOCK? OR STOP? OR RETARD? OR SLOW? OR DE
                LAY? OR LIMIT? OR DECREAS? OR LOWER? OR LESSEN? OR MINIMI
                Z? OR MINIMIS? OR DISRUPT?
L14             QUE  SPE=ON  ABB=ON  PLU=ON  FUNGUS OR FUNGI OR FUNGAL?
L15             QUE  SPE=ON  ABB=ON  PLU=ON  ANTIFUNG? OR FUNGICID? OR FU
                NGISTAT?
L16             QUE  SPE=ON  ABB=ON  PLU=ON  SCREEN? OR TEST OR TESTING O
                R TESTED OR EVALUAT? OR DETERMIN?
L17             QUE  SPE=ON  ABB=ON  PLU=ON  OVEREXPRESS? OR (OVER(1W)EXP
                RESS?)
L18             QUE  SPE=ON  ABB=ON  PLU=ON  PROTEIN
L19             QUE  SPE=ON  ABB=ON  PLU=ON  GWT1 OR (GWT(1W)(1 OR I)) OR
                 GWTI
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```
L20             QUE  SPE=ON  ABB=ON  PLU=ON  GENE
L21             QUE  SPE=ON  ABB=ON  PLU=ON  SACCHAROMYC? OR CEREVIS?
L22             QUE  SPE=ON  ABB=ON  PLU=ON  TEST OR TESTING OR TESTED OR
                 DETECT? OR DETERMIN? OR ANALY? OR SENSE OR SENSED OR SEN
                SING OR BIOSENS? OR ?ASSAY? OR ?MEASUR?
L23             QUE  SPE=ON  ABB=ON  PLU=ON  ANCHOR?
L24             QUE  SPE=ON  ABB=ON  PLU=ON  GPI
L25             QUE  SPE=ON  ABB=ON  PLU=ON  PI
L26             QUE  SPE=ON  ABB=ON  PLU=ON  ?GLYCOS? OR GLC?
L27             QUE  SPE=ON  ABB=ON  PLU=ON  ?PHOSPHATID?
L28             QUE  SPE=ON  ABB=ON  PLU=ON  ?INOSIT?
L29             QUE  SPE=ON  ABB=ON  PLU=ON  (?PHOSPHATID? (1T)?INOSIT?)
                OR (?PHOSPHATID? (1W)?INOSIT?)
L30             QUE  SPE=ON  ABB=ON  PLU=ON  N(1W)ACYL?
L31             QUE  SPE=ON  ABB=ON  PLU=ON  ACYLAT?
L32             QUE  SPE=ON  ABB=ON  PLU=ON  THIN(1W)LAYER
L33             QUE  SPE=ON  ABB=ON  PLU=ON  CHROMATOG?
L34             QUE  SPE=ON  ABB=ON  PLU=ON  TLC
L35             QUE  SPE=ON  ABB=ON  PLU=ON  CELL(2A)(WALL OR SURFACE)
L43          41 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  (GWT1/CNS OR
                (GWT/CNS(1W)(1/CNS OR I/CNS)) OR GWTI/CNS)
L98             QUE  SPE=ON  ABB=ON  PLU=ON  "GWT1 GENE"+PFT,OLD,NEW,NT/C
                T
L99           1 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  L43 OR L98
L100            QUE  SPE=ON  ABB=ON  PLU=ON  "SACCHAROMYCES CEREVISIAE PR
                OTEIN"+PFT,OLD,NEW,NT/CT
L101          5 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  GWT1 OR (GWT(1W)(1 OR
                I)) OR GWTI
L102       1013 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  (L100 OR L21) AND
                ((L24 OR L25) OR L29)
L103       1015 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  L99 OR (L101 OR L102)
L104            QUE  SPE=ON  ABB=ON  PLU=ON  "ANTIFUNGAL ACTIVITY"+PFT,OL
                D,NEW,NT/CT
L105            QUE  SPE=ON  ABB=ON  PLU=ON  "ANTIFUNGAL AGENT"+PFT,OLD,N
                EW,NT/CT
L106            QUE  SPE=ON  ABB=ON  PLU=ON  "DRUG SCREENING"+PFT,OLD,NEW
                ,NT/CT
L107         674 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  L103 AND (L106 OR L16
                OR L22 OR (L33 OR L34))
L108         263 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  L107 AND ((L14 OR L15)
                OR (L104 OR L105))
L109          28 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  L108 AND ((L104 OR
                L105) OR L15)
L110          28 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  L109 AND (L13 OR L14
                OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23
                OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32
                OR L33 OR L34 OR L35)
L111          28 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  (L109 OR L110)
L112           2 SEA FILE=EMBASE SPE=ON  ABB=ON  PLU=ON  L111 AND (L6 OR L7 OR
                L8 OR L9 OR L10 OR L11 OR L12)


=> d his l125

     (FILE 'BIOSIS, CABA, BIOTECHNO, DRUGU, VETU' ENTERED AT 13:07:01 ON 11
     SEP 2009)
L125           0 S L124 AND L6-L12

=> d que l125
L6              QUE  SPE=ON  ABB=ON  PLU=ON  TSUKAHARA, K?/AU,AUTH
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L7              QUE  SPE=ON  ABB=ON  PLU=ON  TSUCHIYA, M?/AU,AUTH
L8              QUE  SPE=ON  ABB=ON  PLU=ON  JIGAMI, Y?/AU,AUTH
L9              QUE  SPE=ON  ABB=ON  PLU=ON  NAKAYAMA, K?/AU,AUTH
L10             QUE  SPE=ON  ABB=ON  PLU=ON  UMEMURA, M?/AU,AUTH
L11             QUE  SPE=ON  ABB=ON  PLU=ON  OKAMOTO, M?/AU,AUTH
L12             QUE  SPE=ON  ABB=ON  PLU=ON  EISAI/CS,SO,PA OR ((NATIONAL
                 (1W)(INST OR INSTITUTE))(5A)(ADVANCED(1W)INDUSTRIAL)(5A)
                (SCIENCE (3W)(TECH OR TECHNOL OR TECHNOLOGY)))/CS,SO,PA
L13             QUE  SPE=ON  ABB=ON  PLU=ON  ANTAGON? OR INHIBIT? OR PROH
                IBIT? OR PREVENT? OR DIMINISH? OR REDUC? OR IMPED? OR DEP
                RESS? OR SUPPRESS? OR REPRESS? OR OBSTRUCT? OR RESTRICT?
                OR TERMINAT? OR BLOCK? OR STOP? OR RETARD? OR SLOW? OR DE
                LAY? OR LIMIT? OR DECREAS? OR LOWER? OR LESSEN? OR MINIMI
                Z? OR MINIMIS? OR DISRUPT?
L14             QUE  SPE=ON  ABB=ON  PLU=ON  FUNGUS OR FUNGI OR FUNGAL?
L15             QUE  SPE=ON  ABB=ON  PLU=ON  ANTIFUNG? OR FUNGICID? OR FU
                NGISTAT?
L16             QUE  SPE=ON  ABB=ON  PLU=ON  SCREEN? OR TEST OR TESTING O
                R TESTED OR EVALUAT? OR DETERMIN?
L17             QUE  SPE=ON  ABB=ON  PLU=ON  OVEREXPRESS? OR (OVER(1W)EXP
                RESS?)
L18             QUE  SPE=ON  ABB=ON  PLU=ON  PROTEIN
L19             QUE  SPE=ON  ABB=ON  PLU=ON  GWT1 OR (GWT(1W)(1 OR I)) OR
                 GWTI
L20             QUE  SPE=ON  ABB=ON  PLU=ON  GENE
L21             QUE  SPE=ON  ABB=ON  PLU=ON  SACCHAROMYC? OR CEREVIS?
L22             QUE  SPE=ON  ABB=ON  PLU=ON  TEST OR TESTING OR TESTED OR
                 DETECT? OR DETERMIN? OR ANALY? OR SENSE OR SENSED OR SEN
                SING OR BIOSENS? OR ?ASSAY? OR ?MEASUR?
L23             QUE  SPE=ON  ABB=ON  PLU=ON  ANCHOR?
L24             QUE  SPE=ON  ABB=ON  PLU=ON  GPI
L25             QUE  SPE=ON  ABB=ON  PLU=ON  PI
L26             QUE  SPE=ON  ABB=ON  PLU=ON  ?GLYCOS? OR GLC?
L27             QUE  SPE=ON  ABB=ON  PLU=ON  ?PHOSPHATID?
L28             QUE  SPE=ON  ABB=ON  PLU=ON  ?INOSIT?
L29             QUE  SPE=ON  ABB=ON  PLU=ON  (?PHOSPHATID? (1T)?INOSIT?)
                OR (?PHOSPHATID? (1W)?INOSIT?)
L30             QUE  SPE=ON  ABB=ON  PLU=ON  N(1W)ACYL?
L31             QUE  SPE=ON  ABB=ON  PLU=ON  ACYLAT?
L32             QUE  SPE=ON  ABB=ON  PLU=ON  THIN(1W)LAYER
L33             QUE  SPE=ON  ABB=ON  PLU=ON  CHROMATOG?
L34             QUE  SPE=ON  ABB=ON  PLU=ON  TLC
L35             QUE  SPE=ON  ABB=ON  PLU=ON  CELL(2A)(WALL OR SURFACE)
L43          41 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  (GWT1/CNS OR
                (GWT/CNS(1W)(1/CNS OR I/CNS)) OR GWTI/CNS)
L114          0 SEA L43
L115         16 SEA L19
L116       2297 SEA L21 AND ((L24 OR L25) OR L29)
L117       2306 SEA (L114 OR L115 OR L116)
L118       1418 SEA L117 AND (L16 OR L22 OR (L33 OR L34))
L119         54 SEA L118 AND (L15 OR (L13(5A) L14))
L120          6 SEA L119 AND (L33 OR L34)
L121          6 SEA L119 AND ((L16 OR L22)(7A)(L15 OR (L13(5A) L14)))
L122         12 SEA L120 OR L121
L123         12 SEA L122 AND (L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR
                L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR
                L29 OR L30 OR L31 OR L32 OR L33 OR L34 OR L35)
L124         12 SEA (L122 OR L123)
L125          0 SEA L124 AND (L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12)
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=> d his l131

     (FILE 'PASCAL, JAPIO, LIFESCI, CEABA-VTB, BIOENG, BIOTECHDS, DRUGB, VETB,
     SCISEARCH, CONFSCI, DISSABS, RDISCLOSURE' ENTERED AT 13:15:09 ON 11 SEP
     2009)
L131          4 S L130 AND L6-L12

=> d que l131
L6              QUE  SPE=ON  ABB=ON  PLU=ON  TSUKAHARA, K?/AU,AUTH
L7              QUE  SPE=ON  ABB=ON  PLU=ON  TSUCHIYA, M?/AU,AUTH
L8              QUE  SPE=ON  ABB=ON  PLU=ON  JIGAMI, Y?/AU,AUTH
L9              QUE  SPE=ON  ABB=ON  PLU=ON  NAKAYAMA, K?/AU,AUTH
L10             QUE  SPE=ON  ABB=ON  PLU=ON  UMEMURA, M?/AU,AUTH
L11             QUE  SPE=ON  ABB=ON  PLU=ON  OKAMOTO, M?/AU,AUTH
L12             QUE  SPE=ON  ABB=ON  PLU=ON  EISAI/CS,SO,PA OR ((NATIONAL
                 (1W)(INST OR INSTITUTE))(5A)(ADVANCED(1W)INDUSTRIAL)(5A)
                (SCIENCE (3W)(TECH OR TECHNOL OR TECHNOLOGY)))/CS,SO,PA
L13             QUE  SPE=ON  ABB=ON  PLU=ON  ANTAGON? OR INHIBIT? OR PROH
                IBIT? OR PREVENT? OR DIMINISH? OR REDUC? OR IMPED? OR DEP
                RESS? OR SUPPRESS? OR REPRESS? OR OBSTRUCT? OR RESTRICT?
                OR TERMINAT? OR BLOCK? OR STOP? OR RETARD? OR SLOW? OR DE
                LAY? OR LIMIT? OR DECREAS? OR LOWER? OR LESSEN? OR MINIMI
                Z? OR MINIMIS? OR DISRUPT?
L14             QUE  SPE=ON  ABB=ON  PLU=ON  FUNGUS OR FUNGI OR FUNGAL?
L15             QUE  SPE=ON  ABB=ON  PLU=ON  ANTIFUNG? OR FUNGICID? OR FU
                NGISTAT?
L16             QUE  SPE=ON  ABB=ON  PLU=ON  SCREEN? OR TEST OR TESTING O
                R TESTED OR EVALUAT? OR DETERMIN?
L19             QUE  SPE=ON  ABB=ON  PLU=ON  GWT1 OR (GWT(1W)(1 OR I)) OR
                 GWTI
L21             QUE  SPE=ON  ABB=ON  PLU=ON  SACCHAROMYC? OR CEREVIS?
L22             QUE  SPE=ON  ABB=ON  PLU=ON  TEST OR TESTING OR TESTED OR
                 DETECT? OR DETERMIN? OR ANALY? OR SENSE OR SENSED OR SEN
                SING OR BIOSENS? OR ?ASSAY? OR ?MEASUR?
L24             QUE  SPE=ON  ABB=ON  PLU=ON  GPI
L25             QUE  SPE=ON  ABB=ON  PLU=ON  PI
L29             QUE  SPE=ON  ABB=ON  PLU=ON  (?PHOSPHATID? (1T)?INOSIT?)
                OR (?PHOSPHATID? (1W)?INOSIT?)
L33             QUE  SPE=ON  ABB=ON  PLU=ON  CHROMATOG?
L34             QUE  SPE=ON  ABB=ON  PLU=ON  TLC
L127         21 SEA L19
L128        588 SEA (L21(10A)((L24 OR L25) OR L29))
L129      29842 SEA (L16 OR L22)(10A)((L13(5A) L14) OR L15)
L130         30 SEA (L127 OR L128) AND (L129 OR (L33 OR L34))
L131          4 SEA L130 AND (L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12)


=> dup rem l62 l78 l96 l112 l125 l131
L125 HAS NO ANSWERS
DUPLICATE IS NOT AVAILABLE IN 'RDISCLOSURE'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
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PROCESSING COMPLETED FOR L62
PROCESSING COMPLETED FOR L78
PROCESSING COMPLETED FOR L96
PROCESSING COMPLETED FOR L112
PROCESSING COMPLETED FOR L125
PROCESSING COMPLETED FOR L131
L136         10 DUP REM L62 L78 L96 L112 L125 L131 (8 DUPLICATES REMOVED)
                ANSWERS '1-5' FROM FILE HCAPLUS
                ANSWERS '6-8' FROM FILE WPIX
                ANSWER '9' FROM FILE MEDLINE
                ANSWER '10' FROM FILE JAPIO


=> file stnguide
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Sep  4, 2009 (20090904/UP).
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=> d ibib ed abs hitind hitstr 1-5
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, WPIX, MEDLINE, JAPIO' - CONTINUE?
(Y)/N:y



L136 ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2009 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2004:468035  HCAPLUS  Full-text
DOCUMENT NUMBER:          141:35948
TITLE:                    Method for screening compound
                          inhibiting enzymatic activity of GWT1
                          gene product
INVENTOR(S):              Tsukahara, Kappei; Tsuchiya, Mamiko
                          ; Jigami, Yoshifumi; Nakayama,
                          Kenichi; Umemura, Mariko; Okamoto,
                          Michiyo
PATENT ASSIGNEE(S):       Eisai Co., Ltd., Japan; National
                          Institute of Advanced
                          Industrial Science and
                          Technology
SOURCE:                   PCT Int. Appl., 94 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2004048604         A1    20040610    WO 2003-JP14909         20031121 <--
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK,
             LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
             OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
             TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2003284635         A1    20040618    AU 2003-284635          20031121 <--
     EP 1564299            A1    20050817    EP 2003-774148          20031121 <--
     EP 1564299            B1    20070620
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     CN 1742095            A     20060301    CN 2003-80109116        20031121 <--
     CN 100371456          C     20080227
     AT 365224             T     20070715    AT 2003-774148          20031121 <--
     JP 4061309            B2    20080319    JP 2004-555006          20031121 <--
     US 20060240429        A1    20061026    US 2005-536935          20050520 <--
PRIORITY APPLN. INFO.:                         JP 2002-339418      A   20021122
                                               WO 2003-JP14909     W   20031121

ED   Entered STN:  10 Jun 2004
AB   A method is provided for screening a compound capable of inhibiting the
     transportation of a GPI anchor protein into fungal cell wall by a convenient
     method of assaying the enzymic transacylation to GlcN-PI using a membrane
     fraction expressing a GWT1 gene product.  A novel antifungal agent can be
     created, which inhibits the process of transporting the GPI anchor protein
```

into cell wall, and thereby, inhibits the synthesis of fungal cell wall as well as the adhesion to host cells.

IC ICM C12Q001-02
ICS G01N033-50; G01N033-15; C12N015-55

CC 9-2 (Biochemical Methods)
Section cross-reference(s): 10

ST antifungal agent screening GWT1 protein inhibition

IT Gene, microbial
Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GWT1; method for screening compound inhibiting enzymic activity of GWT1 protein)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Glycosylphosphatidylinositol-anchored; method for screening compound inhibiting enzymic activity of GWT1 protein)

IT Biological transport
Cell proliferation
Drug screening
Fungi
Fungicides
Membrane, biological
TLC (thin layer chromatography)
(method for screening compound inhibiting enzymic activity of GWT1 protein)

IT Gene expression
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method for screening compound inhibiting enzymic activity of GWT1 protein)

IT DNA sequences
(of fungus GWT1 genes)

IT Protein sequences
(of fungus GWT1 proteins)

IT Glycophospholipids
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(phosphatidylinositol-containing; method for screening compound inhibiting enzymic activity of GWT1 protein)

IT Cell wall
(synthesis; method for screening compound inhibiting enzymic activity of GWT1 protein)

IT Adhesion, biological
(to host cells; method for screening compound inhibiting enzymic activity of GWT1 protein)

IT Acylation
(transacylation, enzymic; method for screening compound inhibiting enzymic activity of GWT1 protein)

IT 702723-62-4, Protein (Saccharomyces cerevisiae GWT1) 702723-64-6, Protein (Candida albicans GWT1) 702723-66-8, Protein (Candida albicans GWT1) 702723-68-0, Protein (Schizosaccharomyces pombe GWT1) 702723-70-4, Protein (Aaperillus fumigatus GWT1) 702723-74-8, Protein (Cryptococcus neoformans

GWT1)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; method for screening compound inhibiting enzymic activity of GWT1 protein)

IT 389805-42-9 561290-69-5 700348-92-1 700348-93-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method for screening compound inhibiting enzymic activity of GWT1 protein)

IT 702723-61-3, DNA (Saccharomyces cerevisiae GWT1 gene) 702723-63-5, DNA (Candida albicans GWT1 gene) 702723-65-7, DNA (Candida albicans GWT1 gene) 702723-67-9 702723-69-1 702723-71-5 702723-72-6 702723-73-7, DNA (Cryptococcus neoformans GWT1 gene)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; method for screening compound inhibiting enzymic activity of GWT1 protein)

IT 702723-88-4 702723-89-5 702723-90-8 702723-91-9
RL: PRP (Properties)
(unclaimed nucleotide sequence; method for screening compound inhibiting enzymic activity of GWT1 gene product)

IT 702723-62-4, Protein (Saccharomyces cerevisiae GWT1) 702723-64-6, Protein (Candida albicans GWT1) 702723-66-8, Protein (Candida albicans GWT1) 702723-68-0, Protein (Schizosaccharomyces pombe GWT1) 702723-70-4, Protein (Aaperillus fumigatus GWT1) 702723-74-8, Protein (Cryptococcus neoformans GWT1)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; method for screening compound inhibiting enzymic activity of GWT1 protein)

RN 702723-62-4 HCAPLUS
CN Protein (Saccharomyces cerevisiae GWT1) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 702723-64-6 HCAPLUS
CN Protein (Candida albicans GWT1) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 702723-66-8 HCAPLUS
CN Protein (Candida albicans GWT1) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 702723-68-0 HCAPLUS
CN Protein (Schizosaccharomyces pombe GWT1) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 702723-70-4 HCAPLUS
CN Protein (Aaperillus fumigatus GWT1) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 702723-74-8 HCAPLUS
CN Protein (Cryptococcus neoformans GWT1) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT 702723-61-3, DNA (Saccharomyces cerevisiae GWT1 gene) 702723-63-5, DNA (Candida albicans GWT1 gene) 702723-65-7, DNA (Candida albicans GWT1 gene) 702723-67-9 702723-69-1 702723-71-5 702723-72-6 702723-73-7, DNA (Cryptococcus neoformans GWT1 gene)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; method for screening compound inhibiting enzymic activity of GWT1 protein)
RN 702723-61-3 HCAPLUS
CN DNA (Saccharomyces cerevisiae GWT1 gene) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 702723-63-5 HCAPLUS
CN DNA (Candida albicans GWT1 gene) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 702723-65-7 HCAPLUS
CN DNA (Candida albicans GWT1 gene) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 702723-67-9 HCAPLUS
CN DNA (Schizosaccharomyces pombe GWT1 gene) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 702723-69-1 HCAPLUS
CN DNA (Aaperillus fumigatus GWT1 gene plus flanks) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 702723-71-5 HCAPLUS
CN DNA (Aaperillus fumigatus GWT1 gene plus flanks) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 702723-72-6 HCAPLUS
CN DNA (Cryptococcus neoformans GWT1 gene plus flanks) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 702723-73-7 HCAPLUS
CN DNA (Cryptococcus neoformans GWT1 gene) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:468008 HCAPLUS Full-text
DOCUMENT NUMBER: 141:34645
TITLE: Methods of screening for compounds that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme
INVENTOR(S): Hata, Katsura; Ogawa, Kaoru; Tsukada, Itaru; Nakamoto,

Kazutaka; Sagane, Koji; Tanaka, Keigo; Tsukahara, Kappei; Horii, Toshihiro

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan

SOURCE: PCT Int. Appl., 214 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004048567	A2	20040610	WO 2003-JP14920	20031121 <--
WO 2004048567	A3	20041014		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2505067	A1	20040610	CA 2003-2505067	20031121 <--
AU 2003282393	A1	20040618	AU 2003-282393	20031121 <--
AU 2003282393	B2	20070705		
EP 1565749	A2	20050824	EP 2003-774152	20031121 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1742203	A	20060301	CN 2003-80109105	20031121 <--
JP 2006506996	T	20060302	JP 2004-555010	20031121 <--
JP 4315907	B2	20090819		
CN 101092627	A	20071226	CN 2007-10104286	20031121 <--
CN 101092628	A	20071226	CN 2007-10104287	20031121 <--
KR 825547	B1	20080425	KR 2005-709212	20050520
US 20060172404	A1	20060803	US 2005-535928	20051209
KR 2007010088	A	20070119	KR 2006-727915	20061229
KR 2007065452	A	20070622	KR 2007-712681	20070605
AU 2007216681	A1	20070927	AU 2007-216681	20070907 <--
AU 2007216681	B2	20081218		
JP 2009077715	A	20090416	JP 2008-242395	20080922 <--
JP 2009183290	A	20090820	JP 2009-71722	20090324 <--

PRIORITY APPLN. INFO.:

US 2002-428589P	P	20021122
AU 2003-282393	A3	20031121
CN 2003-80109105	A3	20031121
JP 2004-555010	A3	20031121
WO 2003-JP14920	W	20031121
KR 2005-709212	A3	20050520

ED Entered STN: 10 Jun 2004

AB The inventors isolated gene GWT1 (PfGWT1), encoding one of the enzymes involved in glycosylphosphatidylinositol (GPI) biosynthesis in the malaria parasite P. falciparum. In addition, the inventors revealed that degenerate mutant DNAs, with a lower AT content than the DNA encoding the PfGWT1 protein , can complement the phenotype of GWT1-deficient yeast. Based on the findings, the present invention provides the GWT1 protein of malaria parasites and the use of the recombinant protein in methods of screening for antimalarial drugs. The present invention also provides degenerate mutant DNAs encoding proteins involved in GPI biosynthesis, and which have a lower AT content than the original DNAs. The present invention also provides methods

of screening for antimalarial drugs which use the degenerate mutant DNAs. Five compds. exhibited antimalarial activity by their ability to inhibit growth of S. cerevisiae expressing gene GWT1 from a plasmid and by their ability to inhibit P. falciparum infection in a red blood cell culture system.

IC ICM C12N015-09
ICS C07K014-445

CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1, 7, 10, 13

ST DNA sequence Plasmodium gene GWT1 glucosamine phosphatidylinositol acyltransferase; Plasmodium gene GWT1 degenerate codon complementation yeast antimalarial screening; sequence synthetic GWT1 GPI synthase gene human Saccharomyces

IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(CDC91; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)

IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(DPM1; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)

IT Gene, animal
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(DPM2; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)

IT Gene, animal
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(DPM3; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)

IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(GAA1; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)

IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(GPI10; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)

IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(GPI11; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)

IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(GPI12; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria

parasites)
IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(GPI13; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)
IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(GPI15; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)
IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(GPI16; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)
IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(GPI17; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)
IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(GPI1; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)
IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(GPI2; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)
IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(GPI3; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)
IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(GPI7; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)
IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(GPI8; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)
IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(GWT1; methods of screening for compds. that inhibit the biosynthesis of

glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT Molecular association
(GWT1p binding compds. or binding inhibitors; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Glycosylphosphatidylinositol (GPI) synthase; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(MCD4; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)

IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(PIG-M; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)

IT Gene, animal
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(SL15; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)

IT Codons
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(degenerate, lower AT content; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT Erythrocyte
(disease, infection; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT Acylation
(enzymic; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT Infection
(erythrocyte; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT Growth, microbial
(inhibition; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT Biological transport

(intracellular, of GPI-anchored proteins, inhibition; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT Antimalarials
Cell wall
Codon usage
Complementation (genetic)
DNA sequences
Drug screening
Drug targets
Genetic engineering
Human
Molecular cloning
Mutagenesis
Nucleic acid hybridization
Plasmodium falciparum
Plasmodium vivax
Protein sequences
Saccharomyces cerevisiae
(methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT Gene, microbial
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(open reading frame, YDR437W; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites)

IT Glycolipoproteins
RL: ANT (Analyte); ANST (Analytical study)
(phosphatidylinositol-containing, cell wall -associated; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT Glycophospholipids
Glycophospholipids
RL: ANT (Analyte); ANST (Analytical study)
(phosphatidylinositol-containing; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT Yeast
(recombinant host; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT Fungi
(transformed; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT 703436-43-5P 703436-67-3P 703436-68-4P 703436-69-5P 703436-70-8P
703436-71-9P 703436-72-0P 703436-73-1P 703436-74-2P 703436-75-3P
703436-76-4P 703436-77-5P 703436-78-6P 703436-79-7P 703436-80-0P
703436-81-1P 703436-82-2P 703436-83-3P 703436-84-4P, Protein
(human gene DPM2 coding region) 703436-85-5P, Protein

(human gene DPM3 coding region) 703436-86-6P, Protein
(human gene SL15 coding region)
RL: BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(amino acid sequence; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT 703436-37-7 703436-41-3
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT 263158-32-3P, Acyltransferase, glucosaminylphosphatidylinositol
RL: BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(gene GWT1; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT 389805-42-9 561290-69-5 704884-58-2 704884-59-3 704884-60-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT 703436-36-6 703436-44-6, DNA (Plasmodium vivax gene GWT1) 703436-45-7 703436-46-8, DNA (Plasmodium falciparum gene GPI1) 703436-47-9, DNA (Plasmodium falciparum gene GPI8) 703436-48-0, DNA (Plasmodium falciparum gene GPI3) 703436-49-1, DNA (Plasmodium falciparum gene GPI10) 703436-50-4, DNA (Plasmodium falciparum gene GPI13)
703436-51-5, DNA (Plasmodium falciparum gene GAA1)
703436-52-6, DNA (Plasmodium falciparum gene DPM1)
703436-53-7, DNA (Plasmodium falciparum gene PIG-M)
703436-54-8, DNA (Saccharomyces cerevisiae gene GPI2) 703436-55-9 703436-56-0 703436-57-1
703436-58-2, DNA (Saccharomyces cerevisiae gene MCD4) 703436-59-3 703436-60-6, DNA (Saccharomyces cerevisiae gene GPI7) 703436-61-7 703436-62-8
703436-63-9 703436-64-0, DNA (human gene DPM2 coding region)
703436-65-1, DNA (human gene DPM3 coding region) 703436-66-2, DNA (human gene SL15 coding region)
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT 703440-37-3 703440-38-4 703440-39-5 703440-40-8 703440-41-9
703440-42-0 703440-43-1 703440-44-2
RL: PRP (Properties)
(unclaimed nucleotide sequence; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)

IT 703436-37-7 703436-41-3

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)
RN 703436-37-7 HCAPLUS
CN Acyltransferase, glucosaminylphosphatidylinositol (Plasmodium falciparum strain 3D7 gene GWT1) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 703436-41-3 HCAPLUS
CN Acyltransferase, glucosaminylphosphatidylinositol (Plasmodium vivax gene GWT1) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT 703436-36-6 703436-44-6, DNA (Plasmodium vivax gene GWT1) 703436-45-7
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; methods of screening for compds. that inhibit the biosynthesis of glycosylphosphatidylinositol in malaria parasites using gene GWT1 and GWT1 enzyme)
RN 703436-36-6 HCAPLUS
CN DNA (Plasmodium falciparum strain 3D7 gene GWT1) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 703436-44-6 HCAPLUS
CN DNA (Plasmodium vivax gene GWT1) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 703436-45-7 HCAPLUS
CN DNA (Plasmodium falciparum clone opfGWT1 gene GWT1 deriv.-specifying) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2003:551751 HCAPLUS Full-text
DOCUMENT NUMBER: 139:111614
TITLE: Method of screening compound having fungal cell wall synthesis inhibitory activity
INVENTOR(S): Tsukahara, Kappei; Sato, Toshitaka; Nakamoto, Kazutaka; Tsuchiya, Mamiko; Sagane, Koji
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 204 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003058233	A1	20030717	WO 2002-JP13807	20021227 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

JP 2005168301	A	20050630	JP 2001-401947	20011228 <--
AU 2002357533	A1	20030724	AU 2002-357533	20021227 <--
PRIORITY APPLN. INFO.:			JP 2001-401947 A	20011228
			WO 2002-JP13807 W	20021227

OTHER SOURCE(S): MARPAT 139:111614

ED Entered STN: 18 Jul 2003

AB By a simple binding assay with the use of a membrane fraction in which GWT1 protein is expressed, a compound inhibiting the transport of GPI anchor protein to fungal cell wall can be screened.

IC ICM G01N033-15
ICS G01N033-50; G01N033-566; A61K045-00; A61P031-10; C07K014-195

CC 1-5 (Pharmacology)
Section cross-reference(s): 28

ST antifungal screening GPI protein transport membrane

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GWT1 microbial gene product; method of screening compound having fungal cell wall synthesis inhibitory activity)

IT Biological transport
Candida albicans
Cell membrane
Cell wall
DNA sequences
Drug screening
Fungicides
Protein sequences
Saccharomyces cerevisiae
(method of screening compound having fungal cell wall synthesis inhibitory activity)

IT Reporter gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method of screening compound having fungal cell wall synthesis inhibitory activity)

IT Glycolipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phosphatidylinositol-containing; method of screening compound having fungal cell wall synthesis inhibitory activity)

IT 562119-26-0 562119-28-2 562119-30-6 562119-32-8
562119-34-0 562119-38-4
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; method of screening compound having fungal cell wall synthesis inhibitory activity)

IT 9001-63-2, Lysozyme

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method of screening compound having fungal cell wall synthesis inhibitory activity)

IT 561290-57-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of screening compound having fungal cell wall synthesis inhibitory activity)

IT 561290-61-7 561290-65-1 561290-69-5 561290-73-1 561290-77-5
561290-83-3 561290-93-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of screening compound having fungal cell wall synthesis inhibitory activity)

IT 1198-30-7, 1-Isoquinolinecarbonitrile 41492-05-1, 1-Bromo-4-butylbenzene
RL: RCT (Reactant); RACT (Reactant or reagent)
(method of screening compound having fungal cell wall synthesis inhibitory activity)

IT 561290-54-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method of screening compound having fungal cell wall synthesis inhibitory activity)

IT 562119-25-9 562119-27-1 562119-29-3 562119-31-7
562119-33-9 562119-35-1 562119-36-2 562119-37-3
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; method of screening compound having fungal cell wall synthesis inhibitory activity)

IT 562124-42-9 562124-43-0 562124-44-1 562124-45-2 562124-46-3
562124-47-4 562124-48-5 562124-49-6 562124-50-9 562124-51-0
562124-52-1 562124-53-2 562124-54-3 562124-55-4 562124-56-5
562124-57-6 562124-58-7 562124-59-8 562124-60-1 562124-61-2
562124-62-3 562124-63-4 562124-64-5 562124-65-6 562124-66-7
562124-67-8 562124-68-9 562124-69-0 562124-70-3 562124-71-4
562124-72-5 562124-73-6 562124-74-7 562124-75-8 562124-76-9
562124-77-0 562124-78-1 562124-79-2 562124-80-5 562124-81-6
562124-82-7 562124-83-8 562124-84-9 562124-85-0 562124-86-1
562124-87-2 562124-88-3 562124-89-4 562124-90-7 562124-91-8
RL: PRP (Properties)
(unclaimed nucleotide sequence; method of screening compound having fungal cell wall synthesis inhibitory activity)

IT 390746-33-5
RL: PRP (Properties)
(unclaimed sequence; method of screening compound having fungal cell wall synthesis inhibitory activity)

IT 562119-26-0
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; method of screening compound having fungal cell wall synthesis inhibitory activity)

RN 562119-26-0 HCAPLUS
CN Protein (Saccharomyces cerevisiae clone WO-03/058233-SEQID2 gene GWT1) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT 562119-25-9
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; method of screening compound having fungal cell wall synthesis inhibitory activity)
RN 562119-25-9 HCAPLUS
CN DNA (Saccharomyces cerevisiae clone WO-03/058233-SEQID1 gene GWT1 protein cDNA) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2003:409320 HCAPLUS Full-text
DOCUMENT NUMBER: 139:194280
TITLE: Medicinal genetics approach towards identifying the molecular target of a novel inhibitor of fungal cell wall assembly
AUTHOR(S): Tsukahara, Kappei; Hata, Katsura; Nakamoto, Kazutaka; Sagane, Koji; Watanabe, Nao-aki; Kuromitsu, Junro; Kai, Junko; Tsuchiya, Mamiko; Ohba, Fuminori; Jigami, Yoshifumi; Yoshimatsu, Kentaro; Nagasu, Takeshi
CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai Co., Ltd, Ibaraki, 300-2635, Japan
SOURCE: Molecular Microbiology (2003), 48(4), 1029-1042
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 29 May 2003
AB Glycosylphosphatidylinositol (GPI)-anchored cell wall mannoproteins are required for the adhesion of pathogenic fungi, such as Candida albicans, to human epithelium. Small mol. inhibitors of the cell surface presentation of GPI-anchored mannoproteins would be promising candidate drugs to block the establishment of fungal infections. Here, we describe a medicinal genetics approach to identifying the gene encoding a novel target protein that is required for the localization of GPI- anchored cell wall mannoproteins. By means of a yeast cell-based screening procedure, we discovered a compound, 1-[4-butylbenzyl]isoquinoline (I), that inhibits cell wall localization of GPI-anchored mannoproteins in Saccharomyces cerevisiae. Treatment of C. albicans cells with this compound resulted in reduced adherence to a rat intestine epithelial cell monolayer. A previously uncharacterized gene YJL091c, named GWT1, was cloned as a dosage-dependent suppressor of the I-induced phenotypes. GWT1 knock-out cells showed similar phenotypes to I-treated wild-type cells in terms of cell wall structure and transcriptional profiles. Two different mutants resistant to I each contained a single missense mutation in the coding region of the GWT1 gene. These results all suggest that the GWT1 gene product is the primary target of the compound
CC 10-6 (Microbial, Algal, and Fungal Biochemistry)
ST gene GWT1 GPI mannoprotein cell wall fungi butylbenzylisoquinoline; sequence gene GWT1 Candida Aspergillus
IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL

(Biological study)
(BWT1; medicinal genetics approach towards identifying the mol. target of a novel inhibitor of fungal cell wall assembly)
IT Saccharomyces cerevisiae
(butylbenzylisoquinoline inhibits cell wall localization of GPI-anchored mannoproteins in Saccharomyces cerevisiae)
IT Adhesion, biological
Aspergillus fumigatus
Candida albicans
Cell wall
DNA sequences
Protein sequences
(medicinal genetics approach towards identifying the mol. target of a novel inhibitor of fungal cell wall assembly)
IT Glycophospholipids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phosphatidylinositol-containing; butylbenzylisoquinoline inhibits cell wall localization of GPI-anchored mannoproteins in fungi)
IT 581988-57-0 581988-58-1
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; medicinal genetics approach towards identifying the mol. target of a novel inhibitor of fungal cell wall assembly)
IT 389805-42-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(butylbenzylisoquinoline inhibits cell wall localization of GPI-anchored mannoproteins in fungi)
IT 503997-29-3 503997-30-6
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; medicinal genetics approach towards identifying the mol. target of a novel inhibitor of fungal cell wall assembly)
IT 581988-57-0 581988-58-1
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; medicinal genetics approach towards identifying the mol. target of a novel inhibitor of fungal cell wall assembly)
RN 581988-57-0 HCAPLUS
CN Protein (Candida albicans strain E81022 gene GWT1) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 581988-58-1 HCAPLUS
CN Protein (Aspergillus fumigatus gene GWT1) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT 503997-29-3 503997-30-6
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; medicinal genetics approach towards identifying the mol. target of a novel inhibitor of fungal cell wall assembly)
RN 503997-29-3 HCAPLUS

CN DNA (Candida albicans strain E81022 gene GWT1) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 503997-30-6 HCAPLUS
CN DNA (Aspergillus fumigatus gene GWT1 plus flanks) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:791638 HCAPLUS Full-text
DOCUMENT NUMBER: 139:319697
TITLE: Development of oligosaccharide synthesis system based on yeast cell surface protein display technology and analysis of cell wall synthesizing components by an in vivo reporter system to detect the localization of cell surface mannoproteins
AUTHOR(S): Jigami, Yoshifumi
CORPORATE SOURCE: Cent. Glycosci., Natl. Inst. Adv. Ind. Sci. Technol., Japan
SOURCE: Nippon Nogei Kagaku Kaishi (2003), 77(10), 994-997
CODEN: NNKKAA; ISSN: 0002-1407
PUBLISHER: Nippon Nogei Kagakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
ED Entered STN: 10 Oct 2003
AB A review on (1) in vitro oligosaccharide synthesis using intact yeast cells that display glycosyltransferase at the cell surface through cell-wall anchored protein Pir, (2) discovery of an antifungal agent 1-(4-butylbenzyl)isoquinoline (BIQ) which inhibits cell wall localization of GPI-anchored proteins in yeast, and (3) involvement of GWT1 gene (the primary target of BIQ) in inositol acylation of GPI anchors.
CC 10-0 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 3, 16
ST review GWT1 gene yeast GPI inositol acylation; antifungal butylbenzylisoquinoline GPI protein cell wall review; glycosyltransferase cell surface oligosaccharide synthesis yeast review
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GWT1; oligosaccharide synthesis using yeast expressing glycosyltransferase at cell surface and involvement of GWT1 gene in inositol acylation of GPI anchors)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(Pir; oligosaccharide synthesis using yeast expressing glycosyltransferase at cell surface and involvement of GWT1 gene in inositol acylation of GPI anchors)
IT Glycoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mannose-containing; oligosaccharide synthesis using yeast expressing

glycosyltransferase at cell surface and involvement of GWT1 gene in inositol acylation of GPI anchors)

IT Cell wall
Fungicides
Yeast
(oligosaccharide synthesis using yeast expressing glycosyltransferase at cell surface and involvement of GWT1 gene in inositol acylation of GPI anchors)

IT Oligosaccharides, preparation
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(oligosaccharide synthesis using yeast expressing glycosyltransferase at cell surface and involvement of GWT1 gene in inositol acylation of GPI anchors)

IT Glycophospholipids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phosphatidylinositol-containing; oligosaccharide synthesis using yeast expressing glycosyltransferase at cell surface and involvement of GWT1 gene in inositol acylation of GPI anchors
)

IT 389805-42-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(oligosaccharide synthesis using yeast expressing glycosyltransferase at cell surface and involvement of GWT1 gene in inositol acylation of GPI anchors)

IT 9033-07-2, Glycosyltransferase
RL: BUU (Biological use, unclassified); CAT (Catalyst use); BIOL (Biological study); USES (Uses)
(oligosaccharide synthesis using yeast expressing glycosyltransferase at cell surface and involvement of GWT1 gene in inositol acylation of GPI anchors)

=> d ifull 6-8
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, WPIX, MEDLINE, JAPIO' - CONTINUE?
(Y)/N:y

L136 ANSWER 6 OF 10 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 2008-M54313 [74] WPIX
DOC. NO. CPI: C2008-388202 [74]
TITLE: Novel DNA encoding ceramide added glycosylphosphatidylinositol (GPI) anchor type protein synthetase comprising alpha and beta subunit, for producing ceramide added GPI anchor type protein , useful in health food and cosmetics
DERWENT CLASS: B04; D13; D16; D21
INVENTOR: FUJITA M; JIGAMI Y; UMEMURA M; YOKOO T
PATENT ASSIGNEE: (DOKU-N) DOKURITSU GYOSEI HOJIN SANGYO GIJUTSU SO
COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
JP 2008220328	A	20080925	(200874)*	JA	40[12]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 2008220328	A	JP 2007-66897	20070315

PRIORITY APPLN. INFO: JP 2007-66897 20070315
INT. PATENT CLASSIF.:
IPC ORIGINAL: A23L0001-30 [N,A]; A23L0001-30 [N,C]; C07K0014-37 [I,C]; C07K0014-395 [I,A]; C12N0001-19 [I,A]; C12N0001-19 [I,C]; C12N0015-09 [I,A]; C12N0015-09 [I,C]; C12N0009-00 [I,A]; C12N0009-00 [I,C]; C12P0013-00 [I,C]; C12P0013-02 [I,A]; C12P0021-02 [I,A]; C12P0021-02 [I,C]; C12Q0001-68 [I,A]; C12Q0001-68 [I,C]
JAP. PATENT CLASSIF.:
MAIN/SEC.: A23L0001-30 Z; C07K0014-395; C12N0001-19; C12N0009-00; C12P0013-02; C12P0021-02 C; C12Q0001-68 A; C12N0015-00 A (ZNA)
MAIN: C12N0015-00 A (ZNA)
SECONDARY: C07K0014-395; C12N0001-19; C12N0009-00; C12P0013-02; C12P0021-02 C; C12Q0001-68 A
ADDITIONAL: A23L0001-30 Z
FTERM CLASSIF.: 4B018; 4B024; 4B050; 4B063; 4B064; 4B065; 4H045; 4B024/AA05; 4H045/AA10; 4H045/AA20; 4H045/AA30; 4B065/AA80.X; 4B065/AA80.Y; 4B065/AA91.Y; 4B065/AB01; 4B065/AC14; 4B064/AE02; 4B064/AG01; 4B065/BA01; 4B024/BA07; 4H045/BA10; 4B024/BA80; 4B024/CA01; 4B024/CA09; 4B024/CA11; 4B064/CA19; 4B024/CA20; 4B065/CA24; 4B065/CA27; 4H045/CA40; 4B065/CA41; 4B065/CA50; 4B050/CC03; 4B064/CC24; 4B064/DA10; 4B024/DA12; 4B064/DA20; 4B050/DD04; 4B050/DD11; 4H045/EA01; 4B024/EA04; 4H045/EA15; 4H045/FA74; 4B024/GA11; 4B024/HA01; 4B024/HA11; 4B018/LB10; 4B050/LL02; 4B050/LL10; 4B018/MD18; 4B018/MD81; 4B018/ME02; 4B018/ME14; 4B063/QA01; 4B063/QA13; 4B063/QQ07; 4B063/QQ08; 4B063/QQ42; 4B063/QQ52; 4B063/QR32; 4B063/QR35; 4B063/QR55; 4B063/QR59; 4B063/QR62; 4B063/QS25; 4B063/QS31; 4B063/QX02

BASIC ABSTRACT:

JP 2008220328 A UPAB: 20081118

NOVELTY - A DNA encoding ceramide added glycosylphosphatidylinositol anchor type protein (GIPC-AP) synthetase comprising alpha -subunit and beta subunit, where the DNA encoding alpha -subunit of GIPC-AP, chosen from DNA encoding amino acid sequence having defined 737, 699 or 699 amino acids (SEQ ID Number 6, 10 or 27) given in the specification, and DNA encoding beta - subunit of GIPC-AP, chosen from DNA encoding amino acid sequence having defined 229, 250, or 315 amino acid (SEQ ID Number 4, 8 or 25) given in the specification, is new.

DETAILED DESCRIPTION - A DNA encoding ceramide added glycosylphosphatidylinositol anchor type protein (GIPC-AP) synthetase comprising alpha -subunit and beta subunit, where the DNA encoding alpha - subunit of GIPC-AP, chosen from DNA encoding amino acid sequence having defined 737, 699 or 699 amino acids (SEQ ID Number 6, 10 or 27) given in the

specification, DNA encoding amino acid sequence of SEQ ID Number 6, 10 or 27 in which one or more amino acids are deleted, substituted or added, DNA comprising base sequence having defined 2214, 2100 or 2100 base pairs (SEQ ID Number 5, 9 or 26) given in the specification, DNA comprising base sequence of SEQ ID Number 5, 9 or 26 in which one or more bases are deleted, substituted or added, DNA hybridizing under stringent condition with DNA having base sequence of SEQ ID Number 5, 9 or 26, DNA having 70% or more homology to base sequence of SEQ ID Number 9 and 26, or DNA having 30% or more homology to base sequence of SEQ ID Number 5, 9 or 26; and DNA encoding beta -subunit of GIPC-AP, chosen from DNA encoding amino acid sequence having defined 229, 250, or 315 amino acid (SEQ ID Number 4, 8 or 25) given in the specification, DNA encoding base sequence of SEQ ID Number 4, 8 or 25 in which one or more amino acids are deleted, substituted or added, DNA comprising base sequence having defined 690, 753 or 948 base pair (SEQ ID Number 3, 7 or 24) given in the specification, DNA having base sequence of SEQ ID Number 3, 7 or 24 in which one or more bases are deleted, substituted or added, DNA hybridizing under stringent condition with DNA having base sequence of SEQ ID Number 3, 7 or 24, DNA exhibiting 70% or more homology to DNA having base sequence of SEQ ID Number 7 and 24, or DNA having 30% or more homology to the base sequence of SEQ ID Number 3, 7 and 24, is new. INDEPENDENT CLAIMS are included for the following:

(1) recombinant vector comprising the above-cited DNA;

(2) transformant obtained by introducing the above-cited recombinant vector;

(3) method of producing the protein composite having ceramide added GPI anchor type protein synthesis enzyme activity, or its alpha -subunit, involves culturing the transformant, and recovering the expression product of the DNA;

(4) protein composite having ceramide added GPI anchor type protein-synthesis enzyme activity, or its alpha -subunit obtained by the above-cited method;

(5) method of producing ceramide added GPI anchor type protein, involves (a) culturing the above-cited transformant, and adding the ceramide with respect to GPI anchor type protein produced by the transformant, (b) protein having protein composite or its alpha -subunit, and ceramide added GPI anchor type protein synthesis enzyme activity is allowed to act with respect to GPI anchor type protein, (c) adding ceramide to protein comprising an amino acid sequence of SEQ ID Number 2, amino acid sequence having amino acid residue at position 218-953 of SEQ ID Number 2 or the above amino acid sequence in which one or more amino acids are deleted, substituted or added, (d) protein coded by DNA having defined 2862 base pair (SEQ ID Number 1) given in the specification, DNA having bases at position 652-2859 of SEQ ID Number 1, or DNA hybridizing under stringent condition with DNA having base sequence of SEQ ID Number 1, (e) introducing the DNA having base sequence of SEQ ID Number 1 into the host, (f) culturing the transformant obtained by introducing the DNA of SEQ ID Number 1 into the host, or (g) protein having alpha -subunit activity and protein having beta -subunit activity of ceramide added GPI anchor type protein-synthesis enzyme, is allowed to act simultaneously with respect to GPI anchor type protein or cell capable of producing GPI anchor type protein ;

(6) ceramide added GPI anchor type protein obtained by the above-cited method;

(7) method of producing ceramide, involves removing the cleavage site and sugar chain portion from ceramide added GPI anchor type protein by enzymatic or chemical method;

(8) method of preparing C-type ceramide containing composition, involves using ceramide added GPI anchor type protein in which the cleavage site and sugar chain has been removed;

(9) a C-type ceramide containing composition obtained by the above-cited method;

(10) method of producing GPI anchor type protein to which diacyl glycerol with saturated fatty acid is added in high purity using the budding yeast, involves introducing a mutation into ceramide added GPI anchor type protein-synthesis enzyme gene or suppressing the expression of gene in the genomic DNA of budding yeast, where the synthesis of ceramide added GPI anchor type protein is inhibited or suppressed;

(11) polynucleotide comprising base sequence of SEQ ID Number 5, 9 or 26, base sequence having defined 41, 28, 42, 47, 77 or 32 base pair (SEQ ID Number 12, 15, 16, 18, 19 or 23) given in the specification, base sequence of SEQ ID Number 3, 7 or 24, or base sequence having defined 37, 47 or 77 base pair (SEQ ID Number 14, 18 or 19) given in the specification, and base sequence of SEQ ID Number 11, 13, 17 or 21;

(12) probe or primer for detecting DNA encoding ceramide added GPI anchor type protein synthesis enzyme or its alpha -subunit or beta -subunit, comprising the above-cited polynucleotide; and

(13) method of screening DNA encoding ceramide added GPI anchor type protein synthesis enzyme and/or its alpha -subunit or beta -subunit, involves using the above-cited probe or primer.

The sequence includes aaaaggatccgcaaacaatcttgaaggct (SEQ ID Number 11), ggaattcatgtaccaggtcccactgac (SEQ ID Number 13), gatttctcgaggaataagtaac (SEQ ID Number 17), and ggggtaccatgctgatcatcaatgggaag (SEQ ID Number 21).

ACTIVITY - Gastrointestinal-Gen. No biological data given.

MECHANISM OF ACTION - None given.

USE - The DNA encoding ceramide added glycosylphosphatidylinositol anchor type protein (GIPC-AP) synthetase is useful for producing ceramide added GPI anchor type protein (claimed) which is useful in health food and pharmaceuticals for regulating intestinal function, and in cosmetics for retaining moisturizing effect of skin.

ADVANTAGE - The highly purified ceramide added GPI anchor type protein can be obtained easily. TECHNOLOGY FOCUS:

BIOTECHNOLOGY - Isolation (claimed): The DNA encoding GIPC-AP synthetase is isolated from yeast Saccharomyces cerevisiae. Preferred Enzyme: The GIPC-AP synthetase produces the glycosylphosphatidylinositol (GPI) anchor type protein in which ceramide (C-type ceramide) which consists of hydroxylated fatty acid chain and phytosphingosine is added. Preferred Method: The ceramide added GPI anchor type protein is produced using the viable yeast cell, where the ceramide added GPI anchor type protein is produced on yeast cell surface or in culture solution. The ceramide production process, involves using phospholipase C or phospholipase D. The budding yeast is cwh43.A gene disrupted strain.

EXTENSION ABSTRACT:

EXAMPLE - No suitable example given.

FILE SEGMENT: CPI

MANUAL CODE: CPI: B04-B01B; B04-E01; B04-E02E; B04-E03E; B04-E05; B04-E08; B04-F0100E; B04-L0800E; B04-N0200E; B11-C08E5; B11-C10; B12-K04F; B14-E10; B14-N17; B14-R01; D03-H01T2B; D03-K03; D03-K04; D05-H09; D05-H12A; D05-H12D1; D05-H12E; D05-H14; D05-H17A3; D05-H17A6; D08-B

L136 ANSWER 7 OF 10 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN

ACCESSION NUMBER: 2008-E38705 [30] WPIX

CROSS REFERENCE: 2009-H36092

TITLE: Novel PER1 or PERLD1 enzyme capable of converting phosphatidyl inositol of glycosylphosphatidyl inositol anchor protein into lysophosphatidyl inositol, useful as

reagent for detecting cancer and screening anticancer agent
DERWENT CLASS: B04; D16; S03
INVENTOR: FUJITA M; JIGAMI Y; UMEMURA M; YOKOO T; CHIKAMI Y; YOKO-O T
PATENT ASSIGNEE: (DOKU-N) DOKURITSU GYOSEI HOJIN SANGYO GIJUTSU SO; (NIIT-C) NAT INST ADVANCED IND SCI & TECHNOLOGY
COUNTRY COUNT: 2

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
JP 2008043234	A	20080228	(200830)*	JA	23[10]	
US 20080233608	A1	20080925	(200866)	EN		
JP 4258672	B2	20090430	(200930)	JA	24	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 2008043234	A	JP 2006-220491	20060811
US 20080233608	A1	US 2007-835249	20070807
JP 4258672	B2	JP 2006-220491	20060811

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
JP 4258672	B2	Previous Publ	JP 2008043234	A

PRIORITY APPLN. INFO: JP 2006-220491 20060811
INT. PATENT CLASSIF.:
IPC ORIGINAL: C07K0016-18 [I,A]; C07K0016-18 [I,C]; C07K0016-40 [I,C]; C07K0016-40 [I,A]; C07K0016-40 [I,C]; C12N0001-00 [I,A]; C12N0001-00 [I,C]; C12N0001-15 [I,A]; C12N0001-15 [I,C]; C12N0001-19 [I,A]; C12N0001-19 [I,C]; C12N0001-21 [I,A]; C12N0001-21 [I,C]; C12N0015-00 [I,A]; C12N0015-00 [I,C]; C12N0015-09 [I,C]; C12N0015-09 [I,A]; C12N0015-09 [I,C]; C12N0015-11 [I,A]; C12N0015-11 [I,C]; C12N0005-10 [I,A]; C12N0005-10 [I,C]; C12N0009-00 [I,A]; C12N0009-00 [I,C]; C12N0009-18 [I,C]; C12N0009-18 [I,A]; C12N0009-18 [I,C]; C12P0021-02 [I,C]; C12P0021-02 [I,A]; C12P0021-02 [I,C]; C12P0021-04 [I,A]; C12P0021-04 [I,C]; C12Q0001-02 [I,C]; C12Q0001-02 [I,A]; C12Q0001-02 [I,C]; C12Q0001-02 [I,C]; C12Q0001-02 [I,A]; C12Q0001-02 [I,C]; G01N0033-15 [I,C]; G01N0033-15 [I,A]; G01N0033-15 [I,C]; G01N0033-50 [I,C]; G01N0033-50 [I,A]; G01N0033-50 [I,C]; G01N0033-53 [I,A]; G01N0033-53 [I,C]
ECLA: C12N0009-18; C12P0007-62; C12P0021-00; C12Q0001-02B; G01N0033-574V2
USCLASS NCLM: 435/029.000
NCLS: 435/069.100; 435/183.000; 435/254.200; 435/320.100; 530/387.100; 536/023.200
JAP. PATENT CLASSIF.:
MAIN/SEC.: C07K0016-40; C12N0001-15; C12N0001-19; C12N0001-21; C12N0005-00 A; C12N0009-18; C12P0021-02 C; C12Q0001-02; G01N0033-15 Z; G01N0033-50 Z; G01N0033-53 D; C12N0015-00 A (ZNA)
MAIN: C12N0015-00 A (ZNA)

SECONDARY: C07K0016-40; C12N0001-15; C12N0001-19; C12N0001-21; C12N0005-00 A; C12N0009-18; C12P0021-02 C; C12Q0001-02; G01N0033-15 Z; G01N0033-50 Z; G01N0033-53 D

FTERM CLASSIF.: 2G045; 2G055; 4B024; 4B050; 4B063; 4B064; 4B065; 4H045; 4B024/AA01; 4H045/AA11; 4B024/AA12; 4H045/AA20; 2G045/AA40; 4B065/AB01; 4B065/AC14; 4B064/AG27; 4B065/BA02; 4H045/BA10; 4B024/BA11; 4B065/BB40; 4B024/CA01; 4B064/CA06; 4H045/CA15; 4B064/CA19; 4B065/CA24; 4B065/CA25; 4B065/CA44; 4B065/CA46; 4B050/CC03; 4B064/CC24; 4B064/DA01; 4B024/DA12; 4B064/DA14; 4H045/DA89; 4B050/DD04; 4H045/EA28; 4H045/EA51; 4B050/EE10; 4H045/FA74; 4B024/GA11; 4B050/LL01; 4B050/LL03; 4B063/QA18; 4B063/QQ95; 4B063/QR69; 4B063/QR76; 4B063/QS24; 4B063/QX01

BASIC ABSTRACT:

JP 2008043234 A UPAB: 20090509

NOVELTY - A PER1 or PERLD1 enzyme protein derived from Saccharomyces cerevisiae, and having an amino acid sequence of a fully defined 357 or 320 amino acid (SEQ ID Number 2 or 4) sequence given in the specification or an amino acid sequence comprising one or more amino acid deletion, substitution or addition in SEQ ID Number 2 or 4, and capable of converting phosphatidyl inositol structure of glycosyiphosphatidyl inositol (GPI) anchor protein into lysophosphatidyl inositol structure, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) enzyme protein having 30% or more homology with the above-mentioned enzyme protein;

(2) gene encoding the PER1 or PERLD1 protein and having base sequence chosen from base sequence of a fully defined 1074 or 963 base pair (SEQ ID Number 1 or 3) sequence given in the specification, and base sequence comprising one or more base deletion, substitution or addition in SEQ ID Number 1 or 3;

(3) recombinant vector comprising the gene;

(4) transformant comprising the recombinant vector;

(5) transformation yeast comprising recombinant vector in which PER1 gene is deleted and PERLD1 gene is inserted;

(6) host for preparation of the transformed yeast;

(7) test agent for screening substance that promotes or inhibits lipid remodeling process of GPI anchor protein, comprising the transformed yeast, PER1 deletion yeast, PER1 high expression yeast or wild-type yeast;

(8) method for screening agent that inhibits or promotes lipid remodeling of GPI anchor protein, involves culturing the transformed yeast, PER1 deletion yeast, PER1 high expression yeast or wild-type yeast in a culture medium containing candidate substance, and measuring the quantity of GPI anchor protein in the external medium or in the detergent-resistant membrane (DRM) fraction;

(9) antibody capable of specifically recognizing PER1 or PERLD1 gene product;

(10) method for detecting abnormality in lipid remodeling process of GPI anchor protein, involves measuring the quantity of GPI anchor protein leaked out from a cell into the external medium; and

(11) method for producing GPI anchor protein, involves culturing cell having lipid modeling process abnormality, and extracting GPI anchor protein leaked out in the external medium.

ACTIVITY - Cytostatic. No biological data given.

MECHANISM OF ACTION - None given.

USE - The enzyme protein is useful as reagent for converting phosphatidyl inositol structure of GPI anchor protein into lysophosphatidyl inositol, and screening a substance that promotes or inhibits the above conversion activity of the enzyme protein, or lipid remodeling

process of GPI anchor protein, where the substance that inhibits the activity is candidate substance for anticancer agent (all claimed), and detecting cancer.

ADVANTAGE - The protein enables efficient screening of anticancer agent, and early detection of cancer.

TECHNOLOGY FOCUS:

BIOTECHNOLOGY - Preparation (disclosed): The PER1 or PERLD1 protein is produced by standard recombinant methods. Preferred Medium: The external medium is blood.

EXTENSION ABSTRACT:

EXAMPLE - Genomic DNA of Saccharomyces cerevisiae (budding yeast) was used as template, and PCR was carried out using primers PER1F 5'-aaaaactagttggaacattgcacaaagg-3' (SEQ ID Number 5), and PER1R-NheI 5'-aaaaaagcttttagctagcgtacaattgtctattaccccaa-3' (SEQ ID Number 6). The amplified product was digested using restriction enzymes SpeI and HindIII and inserted in single copy vector pRS316 for budding yeast. The base sequence was determined. The base sequence of open reading frame had a fully defined 1074 base pair (SEQ ID Number 1) sequence given in the specification. The terminator of GPI7 was inserted in the plasmid, introduced into yeast cell and PER1 gene was expressed in the yeast cell. The PER1 protein had a fully defined 357 amino acid (SEQ ID Number 2) sequence given in the specification. Similarly PERLD1 gene was obtained using primers PERLD1-F 5'-aaaagaattcatggccggcctggcggcg-3' (SEQ ID Number 7) and PERLD1-R 5'-aaaagtcgactcagtccagcttgaacttgtcc-3' (SEQ ID Number 8). The amplified product was digested using restriction enzymes EcoRI and SalI and inserted in multi-copy expression vector Yep352GAP II for budding yeast. The base sequence was determined. The base sequence of an open reading frame had a fully defined 963 base pair (SEQ ID Number 3) sequence given in the specification. The plasmid was introduced into yeast cell and PERLD1 gene was expressed in the yeast cell. The PERLD1 Protein had a fully defined 320 amino acid (SEQ ID Number 4) sequence given in the specification.

FILE SEGMENT: CPI; EPI

MANUAL CODE: CPI: B04-B04D5; B04-E08; B04-F09C0E; B04-G01; B04-N03G0E; B11-C08E; B12-K04A1; B12-K04E3; D05-H09; D05-H12B2; D05-H12E; D05-H14A2
EPI: S03-E09F; S03-E14A1

L136 ANSWER 8 OF 10 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN

ACCESSION NUMBER: 2006-164766 [17] WPIX

CROSS REFERENCE: 2005-306075

DOC. NO. CPI: C2006-055016 [17]

TITLE: Agent for preventing and treating malaria, contains heterocyclic compound, its salt or its hydrate as active ingredient

DERWENT CLASS: B02; B03; C02

INVENTOR: ABE S; HANEDA T; INOUE S; MATSUKURA M; NAKAMOTO K; SAGANE K; TANAKA K; TSUKADA I; UEDA N

PATENT ASSIGNEE: (EISA-C) EISAI CO LTD; (EISA-C) EISAI R & D MANAGEMENT CO LTD

COUNTRY COUNT: 110

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2006016548	A1	20060216	(200617)*	JA	330[0]	
EP 1782811	A1	20070509	(200731)	EN		
IN 2007DN00839	P1	20070803	(200771)	EN		

JP 2006531619 X 20080501 (200832) JA 214

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2006016548 A1		WO 2005-JP14505	20050808
EP 1782811 A1		EP 2005-768893	20050808
EP 1782811 A1		WO 2005-JP14505	20050808
IN 2007DN00839 P1		WO 2005-JP14505	20050808
IN 2007DN00839 P1		IN 2007-DN839	20070131
JP 2006531619 X		WO 2005-JP14505	20050808
JP 2006531619 X		JP 2006-531619	20050808

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1782811	A1	Based on	WO 2006016548	A
JP 2006531619	X	Based on	WO 2006016548	A

PRIORITY APPLN. INFO: JP 2005-82760 20050322
JP 2004-232617 20040809
WO 2004-JP14063 20040927

INT. PATENT CLASSIF.:
MAIN: A61K031-465
SECONDARY: A61K031-47; A61K031-4709; A61P033-06
ADDITIONAL: C07D213-82; C07D405-12; C07D409-12
IPC ORIGINAL: A61K0031-455 [I,A]; A61K0031-455 [I,C]; A61K0031-465 [I,A]; A61K0031-465 [I,C]; A61K0031-47 [I,A]; A61K0031-47 [I,C]; A61K0031-4709 [I,A]; A61K0031-4709 [I,C]; A61P0033-00 [I,C]; A61P0033-06 [I,A]; C07D0213-00 [N,C]; C07D0213-00 [I,C]; C07D0213-82 [N,A]; C07D0213-82 [I,A]; C07D0405-00 [N,C]; C07D0405-12 [N,A]; C07D0409-00 [N,C]; C07D0409-12 [N,A]
ECLA: A61K0031-465; A61K0031-47; A61K0031-4709

BASIC ABSTRACT:

WO 2006016548 A1 UPAB: 20060310

NOVELTY - An antimalarial agent contains heterocyclic compound (I-a), its salt or its hydrate as active ingredient.

DETAILED DESCRIPTION - An antimalarial agent contains a heterocyclic compound of formula A1-X1-CH2-E (Ia), its salt or its hydrate as active ingredient.

A1=3-pyridyl or 6-quinolyl (both optionally substituted by 1-3 a1 or a2);

X1=-C(=Y1)-NH-;

Y1=O;

E=furyl, thienyl or phenyl (all optionally substituted by 1-2 a1 or a2);

a1=halo, OH, SH, CN, carboxyl, amino, carbamoyl, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-8C cycloalkyl, 6-10C aryl, 5-10 membered heterocycle, 3-8C cycloalkyl-1-6C alkyl, 3-8C cycloalkylidene-1-6C alkyl, 6-10C aryl-1-6C alkyl, 5-10 membered heterocycle-1-6C alkyl, 1-6C alkoxy, 2-6C alkenyloxy, 2-6C alkynyloxy, 3-8C cycloalkoxy, 6-10C aryloxy, 3-8C cycloalkyl-1-6C alkoxy, 6-10C aryl-1-6C alkoxy, 5-10 membered heterocycle-1-6C alkoxy, 1-6C alkylthio, 2-6C alkenylthio, 2-6C alkynylthio, 3-8C cycloalkylthio, 6-10C arylthio, 3-8C cycloalkyl-1-6C alkylthio, 6-10C aryl-1-6C alkylthio, 5-10 membered heterocycle-1-6C alkylthio, 1-6C alkylamino, 2-6C alkenylamino, 2-6C alkynylamino, 3-8C cycloalkylamino, 6-10C arylamino, 3-8C cycloalkyl-1-6C alkylamino, 6-10C aryl-1-6C alkylamino, 5-10 membered heterocycle-1-6C

alkylamino, di-1-6C alkylamino, N-2-6C alkenyl-N-1-6C alkylamino, N-2-6C alkynyl-N-1-6C alkylamino, N-3-8C cycloalkyl-N-1-6C alkylamino, N-6-10C aryl-N-1-6C alkylamino, N-3-8C cycloalkyl-1-6C alkyl-N-1-6C alkylamino, N-6-10C aryl-1-6C alkyl-N-1-6C alkylamino, N-5-10 membered heterocycle-1-6C alkyl-N-1-6C alkylamino, 1-6C alkylcarbonyl, 1-6C alkoxycarbonyl, 1-6C alkylsulfonyl or -C(=N-Ra1)Ra2;

Ra1=hydroxyl or 1-6C alkoxy;

Ra2=1-6C alkyl;

a2=1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-8C cycloalkyl, 6-10C aryl, 5-10 membered heterocycle, 3-8C cycloalkyl-1-6C alkyl, 6-10C aryl-1-6C alkyl, 5-10 membered heterocycle-1-6C alkyl, 1-6C alkoxy, 2-6C alkenyloxy, 2-6C alkynyloxy, 3-8C cycloalkoxy, 6-10C aryloxy, 3-8C cycloalkyl-1-6C alkoxy, 6-10C aryl-1-6C alkoxy, 5-10 membered heterocycle-1-6C alkoxy, 1-6C alkylthio, 2-6C alkenylthio, 2-6C alkynylthio, 3-8C cycloalkylthio, 6-10C arylthio, 3-8C cycloalkyl-1-6C alkylthio, 6-10C aryl-1-6C alkylthio, 5-10 membered heterocycle-1-6C alkylthio, 1-6C alkylamino, 2-6C alkenylamino, 2-6C alkynylamino, 3-8C cycloalkylamino, 6-10C arylamino, 3-8C cycloalkyl-1-6C alkylamino, 6-10C aryl-1-6C alkylamino, 5-10 membered heterocycle-1-6C alkylamino, di-1-6C alkylamino, N-2-6C alkenyl-N-1-6C alkylamino, N-2-6C alkenyl-N-1-6C alkylamino, N-2-6C alkynyl-N-1-6C alkylamino, N-3-8C cycloalkyl-N-1-6C alkylamino, N-6-10C aryl-N-1-6C alkylamino, N-3-8C cycloalkyl-1-6C alkyl-N-1-6C alkylamino, N-6-10C aryl-1-6C alkyl-N-1-6C alkylamino or N-5-10 membered heterocycle-1-6C alkyl-N-1-6C alkylamino (all optionally substituted by 1-3 b1); and

b1=halo, OH, SH, CN, carboxyl, amino, carbamoyl, nitro, 1-6C alkyl, 3-8C cycloalkyl, 6-10C aryl, 5-10 membered heterocycle, 1-6C alkoxy, 6-10C aryloxy, 5-10 membered heterocyclyloxy, 1-6C alkylcarbonyl, 1-6C alkoxycarbonyl, 1-6C alkylsulfonyl, trifluoromethyl, trifluoromethoxy, 1-6C alkylamino, di-1-6C alkylamino, 6-10C aryl amino, amino-6-10C aryl amino or N-6-10C aryl-1-6C alkyl-N-1-6C alkylamino (optionally substituted by amino, trifluoromethyl, trifluoromethoxy or 1-6C alkyl).

ACTIVITY - Antimalarial. OpfGWT1 expression yeast was cultured in SD culture medium in presence of 2-amino-6-chloronicotinic acid (50 mul/well) at 30degreesC for 2 days. Then, absorbency of turbidity was measured at 660 nm, and antimalarial activity was evaluated by measuring minimum inhibitory concentration (MIC). MIC of the test compound with respect to Plasmodium falciparum (GWT1) strain was found to be 6.25 micrograms/ml.

MECHANISM OF ACTION - GPI-Inhibitor. No biological data given.

USE - For preventing and treating malaria (claimed).

ADVANTAGE - The agent has excellent antimalarial activity, and is highly safe to use. The agent effectively inhibits biosynthesis of glycosyl phosphatidyl inositol by inhibiting the activity of GWT1 gene product of Plasmodium.

EXTENSION ABSTRACT:

DEFINITIONS - Preferred Definitions: - A1=3-pyridyl or 6-quinolyl (optionally substituted with c1, c2, c'1 or c'2); - c1=halo, amino, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-8C cycloalkyl, 6-10C aryl, 5-10 membered heterocycle, 3-8C cycloalkyl-1-6C alkyl, 6-10C aryl-1-6C alkyl, 5-10 membered heterocycle-1-6C alkyl, 1-6C alkoxy, 2-6C alkenyloxy, 2-6C alkynyloxy, 3-8C cycloalkyl-1-6C alkoxy, 6-10C aryl-1-6C alkoxy, 5-10 membered heterocycle-1-6C alkoxy, 1-6C alkylamino, 2-6C alkenylamino, 2-6C alkynylamino, 3-8C cycloalkylamino, 6-10C arylamino, 3-8C cycloalkyl-1-6C alkylamino, 6-10C aryl-1-6C alkylamino, 5-10 membered heterocycle-1-6C alkylamino, 1-6C alkylcarbonyl or -C(=N- OH) Ra2; - c2=amino or c1 (optionally substituted by halo, OH, carboxyl, amino, carbamoyl, 1-6C alkoxy, 1-6C alkylamino, di-1-6C alkylamino, 6-10C arylamino (optionally substituted by amino) or N-6-10C aryl 1-6C alkyl-N-1-6C alkylamino (optionally substituted by amino); - c'1=halo, amino, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 1-6C alkoxy, 2-6C alkenyloxy, 2-6C alkynyloxy, 1-6C alkylamino, 2-6C alkenylamino, 2-6C

alkynylamino or 1-6C alkylcarbonyl; - c'2=1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 1-6C alkoxy, 2-6C alkenyloxy, 2-6C alkynyloxy, 1-6C alkylamino, 2-6C alkenyl amino or 2-6C alkynylamino (all optionally substituted by halo, OH, carboxyl, amino, carbamoyl or 1-6C alkoxy), preferably compound of formula (I); - R1=H, amino, methoxy, methyl, ethynyl, ethoxy, ethylamino, methylcarbonyl or fluoroethyl;and - E=furyl, thienyl or phenyl (optionally substituted by 1-6C alkoxy-1-6C alkyl, 1-6C alkoxy, phenoxy optionally substituted by benzyl, phenyl 1-6C alkyl, halo, 1-6C (halo)alkyl, benzyl optionally substituted by fluorine, chlorine and methyl, n-butoxy methyl or n-butoxy, preferably n-butoxy methyl or n-butoxy.

ADMINISTRATION - The oral dose of antimalarial agent is 1-10000 (10-2000) mg/day/adult. The parenteral dose of antimalarial agent is 0.1-10000 (1-2000) mg/day/adult, in single or divided doses.

EXAMPLE - 2,6-dichloronicotinic acid (40 g), acetamide (80 g) and tris (2-(2-methoxy ethoxy) ethyl) amine (3 ml) were added to mixture of potassium carbonate (78 g), copper chloride (0.93 g) and xylene (80 ml), and stirred at 145degreesC. Further, copper (I) chloride (0.6 g) was added to the reaction solution, and stirred at 145degreesC. The reaction liquid was cooled at 105degreesC. Subsequently, water (100 ml) was added and stirred at room temperature for 1 hour. Finally, hydrochloric acid (150 ml) was added, extracted with ethyl acetate, washed and purified to obtain 2-amino-6-chloro nicotinic acid (1.4 g).

FILE SEGMENT: CPI
MANUAL CODE: CPI: B06-H; B07-D04C; B14-A03B; C06-H; C07-D04C; C14-A03B

=> d bib ed ab ind 9-10
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, WPIX, MEDLINE, JAPIO' - CONTINUE?
(Y)/N:y

L136 ANSWER 9 OF 10 MEDLINE on STN DUPLICATE 4
AN 2003302641 MEDLINE Full-text
DN PubMed ID: 12714589
TI GWT1 gene is required for inositol acylation of glycosylphosphatidylinositol anchors in yeast.
AU Umemura Mariko; Okamoto Michiyo; Nakayama Ken-ichi; Sagane Koji; Tsukahara Kappei; Hata Katsura; Jigami Yoshifumi
CS Research Center for Glycoscience, National Institute of Advanced Industrial Science and Technology, Tsukuba Central 6, Higashi 1-1-1, Tsukuba, Ibaraki 305-8566, Japan.
NC AI147079 (United States NIAID NIH HHS)
U01 AI47087 (United States NIAID NIH HHS)
U01 AI48594 (United States NIAID NIH HHS)
SO The Journal of biological chemistry, (2003 Jun 27) Vol. 278, No. 26, pp. 23639-47. Electronic Publication: 2003-04-24.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
OS GENBANK-AB092505
EM 200308
ED Entered STN: 1 Jul 2003

Last Updated on STN: 21 Aug 2003
Entered Medline: 20 Aug 2003
ED Entered STN: 1 Jul 2003
Last Updated on STN: 21 Aug 2003
Entered Medline: 20 Aug 2003
AB Glycosylphosphatidylinositol (GPI) is a conserved post-translational modification to anchor cell surface proteins to plasma membrane in all eukaryotes. In yeast, GPI mediates cross-linking of cell wall mannoproteins to beta1,6-glucan. We reported previously that the GWT1 gene product is a target of the novel anti-fungal compound, 1-[4-butylbenzyl]isoquinoline, that inhibits cell wall localization of GPI-anchored mannoproteins in Saccharomyces cerevisiae (Tsukahara, K., Hata, K., Sagane, K., Watanabe, N., Kuromitsu, J., Kai, J., Tsuchiya, M., Ohba, F., Jigami, Y., Yoshimatsu, K., and Nagasu, T. (2003) Mol. Microbiol. 48, 1029-1042). In the present study, to analyze the function of the Gwt1 protein, we isolated temperature-sensitive gwt1 mutants. The gwt1 cells were normal in transport of invertase and carboxypeptidase Y but were delayed in transport of GPI -anchored protein, Gas1p, and were defective in its maturation from the endoplasmic reticulum to the Golgi. The incorporation of inositol into GPI-anchored proteins was reduced in gwt1 mutant, indicating involvement of GWT1 in GPI biosynthesis. We analyzed the early steps of GPI biosynthesis in vitro by using membranes prepared from gwt1 and Deltagwt1 cells. The synthetic activity of GlcN-(acyl)PI from GlcN-PI was defective in these cells, whereas Deltagwt1 cells harboring GWT1 gene restored the activity, indicating that GWT1 is required for acylation of inositol during the GPI synthetic pathway. We further cloned GWT1 homologues in other yeasts, Cryptococcus neoformans and Schizosaccharomyces pombe, and confirmed that the specificity of acyl-CoA in inositol acylation , as reported in studies of endogenous membranes (Franzot, S. P., and Doering, T. L. (1999) Biochem. J. 340, 25-32), is due to the properties of Gwt1p itself and not to other membrane components.
CT Acyl Coenzyme A: ME, metabolism
Acylation
Amino Acid Sequence
*Glycosylphosphatidylinositols: BI, biosynthesis
Glycosylphosphatidylinositols: ME, metabolism
Inositol: ME, metabolism
Molecular Sequence Data
Mutation
Protein Transport
*Saccharomyces cerevisiae Proteins: GE, genetics
Saccharomyces cerevisiae Proteins: PH, physiology
Sequence Alignment
Substrate Specificity
Temperature
*Yeasts: ME, metabolism
RN 6917-35-7 (Inositol)
CN 0 (Acyl Coenzyme A); 0 (GWT1 protein, S cerevisiae); 0 (Glycosylphosphatidylinositols); 0 (Saccharomyces cerevisiae Proteins)

L136 ANSWER 10 OF 10 JAPIO (C) 2009 JPO on STN
AN 2005-168301 JAPIO Full-text
TI METHOD FOR SCREENING COMPOUND HAVING FUNGAL CELL WALL SYNTHESIS-INHIBITING ACTIVITY
IN TSUKAHARA KATSUHEI; SATO TOSHITAKA; NAKAMOTO KAZUTAKA; TSUCHIYA MAMIKO
PA EISAI CO LTD
PI JP 2005168301 A 20050630 Heisei
AI JP 2001-401947 (JP2001401947 Heisei) 20011228
PRAI JP 2001-401947 20011228

SO PATENT ABSTRACTS OF JAPAN (CD-ROM), Unexamined Applications, Vol. 2005
ED 20051004
AB PROBLEM TO BE SOLVED: To develop an antifungal agent which inhibits the transport of a GPI (glycorylphosphatidylinositol) anchor protein to a fungal cell wall to prevent the synthesis of the fungal cell wall and thereby inhibits the adhesion to a host cell to prevent the pathogenic fungus from exhibiting the pathogenicity. SOLUTION: A compound for inhibiting the transport of the GPI anchor protein to the fungal cell wall can be screened by a simple Binding assay using a membrane fraction expressing GWT1 protein (a GWT1 gene product).
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IC ICM C12Q001-02
ICS G01N033-15; G01N033-50
ICA C12N015-09

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     FILE 'ZCAPLUS' ENTERED AT 12:04:41 ON 11 SEP 2009
                E US2006-536935/APPS
                E WO2003-14909/APPS
                E WO2003-JP14909/APPS

     FILE 'HCAPLUS' ENTERED AT 12:05:17 ON 11 SEP 2009
L1             1 SEA SPE=ON  ABB=ON  PLU=ON  WO2003-JP14909/APPS
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 12:05:24 ON 11 SEP 2009

     FILE 'WPIX' ENTERED AT 12:09:16 ON 11 SEP 2009
L2             1 SEA SPE=ON  ABB=ON  PLU=ON  WO2003-JP14909/APPS
                D IALL CODE

     FILE 'ZCAPLUS' ENTERED AT 12:09:59 ON 11 SEP 2009
L3             QUE SPE=ON  ABB=ON  PLU=ON  G01N0033/IPC

     FILE 'REGISTRY' ENTERED AT 12:10:40 ON 11 SEP 2009

     FILE 'HCAPLUS' ENTERED AT 12:10:45 ON 11 SEP 2009
L4             TRA PLU=ON  L1 1- RN :      22 TERMS

     FILE 'REGISTRY' ENTERED AT 12:10:45 ON 11 SEP 2009
L5            22 SEA SPE=ON  ABB=ON  PLU=ON  L4

     FILE 'ZCAPLUS' ENTERED AT 12:10:59 ON 11 SEP 2009
L6             QUE SPE=ON  ABB=ON  PLU=ON  TSUKAHARA, K?/AU,AUTH
L7             QUE SPE=ON  ABB=ON  PLU=ON  TSUCHIYA, M?/AU,AUTH
L8             QUE SPE=ON  ABB=ON  PLU=ON  JIGAMI, Y?/AU,AUTH
L9             QUE SPE=ON  ABB=ON  PLU=ON  NAKAYAMA, K?/AU,AUTH
L10            QUE SPE=ON  ABB=ON  PLU=ON  UMEMURA, M?/AU,AUTH
L11            QUE SPE=ON  ABB=ON  PLU=ON  OKAMOTO, M?/AU,AUTH
L12            QUE SPE=ON  ABB=ON  PLU=ON  EISAI/CS,SO,PA OR ((NATIONAL
               (1W)(INST OR INSTITUTE))(5A)(ADVANCED(1W)INDUSTRIAL)(5A)(SCIENC
               E (3W)(TECH OR TECHNOL OR TECHNOLOGY)))/CS,SO,PA
L13            QUE SPE=ON  ABB=ON  PLU=ON  ANTAGON? OR INHIBIT? OR PROHIBIT?
               OR PREVENT? OR DIMINISH? OR REDUC? OR IMPED? OR DEPRESS? OR
               SUPPRESS? OR REPRESS? OR OBSTRUCT? OR RESTRICT? OR TERMINAT?
               OR BLOCK? OR STOP? OR RETARD? OR SLOW? OR DELAY? OR LIMIT? OR
               DECREAS? OR LOWER? OR LESSEN? OR MINIMIZ? OR MINIMIS? OR
               DISRUPT?
L14            QUE SPE=ON  ABB=ON  PLU=ON  FUNGUS OR FUNGI OR FUNGAL?
L15            QUE SPE=ON  ABB=ON  PLU=ON  ANTIFUNG? OR FUNGICID? OR FUNGISTAT
               ?
L16            QUE SPE=ON  ABB=ON  PLU=ON  SCREEN? OR TEST OR TESTING OR
               TESTED OR EVALUAT? OR DETERMIN?
L17            QUE SPE=ON  ABB=ON  PLU=ON  OVEREXPRESS? OR (OVER(1W)EXPRESS?)

L18            QUE SPE=ON  ABB=ON  PLU=ON  PROTEIN
L19            QUE SPE=ON  ABB=ON  PLU=ON  GWT1 OR (GWT(1W)(1 OR I)) OR GWTI
L20            QUE SPE=ON  ABB=ON  PLU=ON  GENE
L21            QUE SPE=ON  ABB=ON  PLU=ON  SACCHAROMYC? OR CEREVIS?
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L22             QUE SPE=ON  ABB=ON  PLU=ON  TEST OR TESTING OR TESTED OR
                DETECT? OR DETERMIN? OR ANALY? OR SENSE OR SENSED OR SENSING
                OR BIOSENS? OR ?ASSAY? OR ?MEASUR?
L23             QUE SPE=ON  ABB=ON  PLU=ON  ANCHOR?
L24             QUE SPE=ON  ABB=ON  PLU=ON  GPI
L25             QUE SPE=ON  ABB=ON  PLU=ON  PI
L26             QUE SPE=ON  ABB=ON  PLU=ON  ?GLYCOS? OR GLC?
L27             QUE SPE=ON  ABB=ON  PLU=ON  ?PHOSPHATID?
L28             QUE SPE=ON  ABB=ON  PLU=ON  ?INOSIT?
L29             QUE SPE=ON  ABB=ON  PLU=ON  (?PHOSPHATID? (1T)?INOSIT?) OR
                (?PHOSPHATID? (1W)?INOSIT?)
L30             QUE SPE=ON  ABB=ON  PLU=ON  N(1W)ACYL?
L31             QUE SPE=ON  ABB=ON  PLU=ON  ACYLAT?
L32             QUE SPE=ON  ABB=ON  PLU=ON  THIN(1W)LAYER
L33             QUE SPE=ON  ABB=ON  PLU=ON  CHROMATOG?
L34             QUE SPE=ON  ABB=ON  PLU=ON  TLC
L35             QUE SPE=ON  ABB=ON  PLU=ON  CELL(2A)(WALL OR SURFACE)
L36             QUE SPE=ON  ABB=ON  PLU=ON  PROTEINS+PFT,OLD,NEW/CT
L37             QUE SPE=ON  ABB=ON  PLU=ON  "GENE EXPRESSION"+PFT,OLD,NEW,NT/CT

L38             QUE SPE=ON  ABB=ON  PLU=ON  "DRUG SCREENING"+PFT,OLD,NEW,NT/CT

L39             QUE SPE=ON  ABB=ON  PLU=ON  FUNGI+PFT,OLD,NEW/CT
L40             QUE SPE=ON  ABB=ON  PLU=ON  FUNGICIDES+PFT,OLD,NEW/CT
L41             QUE SPE=ON  ABB=ON  PLU=ON  GLYCOPHOSPHOLIPIDS+PFT,OLD,NEW/CT
L42             QUE SPE=ON  ABB=ON  PLU=ON  ACYLATION+PFT,OLD,NEW/CT

    FILE 'REGISTRY' ENTERED AT 12:16:33 ON 11 SEP 2009
L43          41 SEA SPE=ON  ABB=ON  PLU=ON  (GWT1/CNS OR (GWT/CNS(1W)(1/CNS OR
                I/CNS)) OR GWTI/CNS)

    FILE 'STNGUIDE' ENTERED AT 12:17:36 ON 11 SEP 2009

    FILE 'HCAPLUS' ENTERED AT 12:19:56 ON 11 SEP 2009
L44           6 SEA SPE=ON  ABB=ON  PLU=ON  L43
L45         331 SEA SPE=ON  ABB=ON  PLU=ON  L41 (L)(L24 OR L25)
L46           4 SEA SPE=ON  ABB=ON  PLU=ON  (L44 OR L45) (L)(L16 (L) L13)
L47          21 SEA SPE=ON  ABB=ON  PLU=ON  (L44 OR L45) (L)L13
L48          37 SEA SPE=ON  ABB=ON  PLU=ON  L45 AND (L19 OR L21)
L49          56 SEA SPE=ON  ABB=ON  PLU=ON  (L46 OR L47 OR L48)
L50          36 SEA SPE=ON  ABB=ON  PLU=ON  L49 AND ((L14 OR L15) OR (L39 OR
                L40) OR L38 OR L16 OR L22)
L51           1 SEA SPE=ON  ABB=ON  PLU=ON  L50 AND (L33 OR L34)
L52          56 SEA SPE=ON  ABB=ON  PLU=ON  (L49 OR L50)
L53             QUE SPE=ON  ABB=ON  PLU=ON  CHROMATOGRAPHY+PFT,OLD,NEW,NT/CT
L54           1 SEA SPE=ON  ABB=ON  PLU=ON  L52 AND (L53 OR (L33 OR L34))
L55          56 SEA SPE=ON  ABB=ON  PLU=ON  L52 OR L54
L56          12 SEA SPE=ON  ABB=ON  PLU=ON  L55 AND ((L14 OR L15) OR (L39 OR
                L40))
L57          12 SEA SPE=ON  ABB=ON  PLU=ON  L51 OR L54 OR L56
L58           4 SEA SPE=ON  ABB=ON  PLU=ON  L3 AND L57
L59          12 SEA SPE=ON  ABB=ON  PLU=ON  (L57 OR L58)
L60          12 SEA SPE=ON  ABB=ON  PLU=ON  L59 AND ((L13 OR L14 OR L15 OR L16
                OR L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR L24 OR L25
                OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33 OR L34
                OR L35) OR (L36 OR L37 OR L38 OR L39 OR L40 OR L41 OR L42))
L61          12 SEA SPE=ON  ABB=ON  PLU=ON  (L59 OR L60)
L62           5 SEA SPE=ON  ABB=ON  PLU=ON  L61 AND (L6 OR L7 OR L8 OR L9 OR
                L10 OR L11 OR L12)
                D BIB 1-5
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L63           7 SEA SPE=ON  ABB=ON  PLU=ON  L61 NOT L62

     FILE 'ZCAPLUS' ENTERED AT 12:32:07 ON 11 SEP 2009
L64             QUE SPE=ON  ABB=ON  PLU=ON  AY<2003 OR PY<2003 OR PRY<2003 OR
                MY<2003 OR REVIEW/DT

     FILE 'HCAPLUS' ENTERED AT 12:32:45 ON 11 SEP 2009
L65           2 SEA SPE=ON  ABB=ON  PLU=ON  L63 AND L64
                D SCAN TI HIT
L66           2 SEA SPE=ON  ABB=ON  PLU=ON  L65 AND GPI/TI
L67           1 SEA SPE=ON  ABB=ON  PLU=ON  L65 AND SCREEN/TI
                D BIB
                D ABS

     FILE 'STNGUIDE' ENTERED AT 12:34:15 ON 11 SEP 2009

     FILE 'WPIX' ENTERED AT 12:34:31 ON 11 SEP 2009
L68        2681 SEA SPE=ON  ABB=ON  PLU=ON  L13 (7A)(L19 OR (L24 OR L25) OR
                L29)
L69         209 SEA SPE=ON  ABB=ON  PLU=ON  L68 AND L3
L70         418 SEA SPE=ON  ABB=ON  PLU=ON  L68 (15A)(L16 OR L22)
L71         552 SEA SPE=ON  ABB=ON  PLU=ON  (L69 OR L70)
                D TRI 1-3
L72          10 SEA SPE=ON  ABB=ON  PLU=ON  L71 AND (L19 OR L21)
                D TRI 1-10
L73         102 SEA SPE=ON  ABB=ON  PLU=ON  L68 AND ((L13(5A)L24) OR L15)
L74           7 SEA SPE=ON  ABB=ON  PLU=ON  L73 AND  (L19 OR L21)
                D TRI 1-7
L75          12 SEA SPE=ON  ABB=ON  PLU=ON  L72 OR L74
L76          12 SEA SPE=ON  ABB=ON  PLU=ON  L75 AND (L13 OR L14 OR L15 OR L16
                OR L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR L24 OR L25
                OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33 OR L34
                OR L35)
L77          12 SEA SPE=ON  ABB=ON  PLU=ON  (L75 OR L76)
L78           6 SEA SPE=ON  ABB=ON  PLU=ON  L77 AND (L6 OR L7 OR L8 OR L9 OR
                L10 OR L11 OR L12)
L79           6 SEA SPE=ON  ABB=ON  PLU=ON  L77 NOT L78
L80           3 SEA SPE=ON  ABB=ON  PLU=ON  L79 AND L64
                D TRI 1-3
                D KWIC 2-3

     FILE 'STNGUIDE' ENTERED AT 12:44:18 ON 11 SEP 2009

     FILE 'MEDLINE' ENTERED AT 12:44:24 ON 11 SEP 2009
L81           0 SEA SPE=ON  ABB=ON  PLU=ON  L43
                E GWT1/CT
                E SACCHAROMYC/CT
                E E54+ALL
L82             QUE SPE=ON  ABB=ON  PLU=ON  "SACCHAROMYCES CEREVISIAE PROTEINS"
                +PFT,OLD,NEW,NT/CT
L83        1958 SEA SPE=ON  ABB=ON  PLU=ON  (L82 OR L21) AND (L19 OR (L24 OR
                L25) OR L29)
                E ANTIFUNG/CT
L84             QUE SPE=ON  ABB=ON  PLU=ON  "ANTIFUNGAL AGENTS"+PFT,OLD,NEW/CT

                E SCREENING/CT
                E E89+ALL
L85             QUE SPE=ON  ABB=ON  PLU=ON  "DRUG EVALUATION, PRECLINICAL"+PFT,
                OLD,NEW,NT/CT
L86        1958 SEA SPE=ON  ABB=ON  PLU=ON  L81 OR L83
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L*** DEL    218 S L86 AND (L83(L)AN/CT)
L87          14 SEA SPE=ON  ABB=ON  PLU=ON  L86 AND (L82(L)AN/CT)
                D TRI 1-14
L88        1386 SEA SPE=ON  ABB=ON  PLU=ON  L86 AND (L84 OR L85 OR L16 OR L22
                OR L33 OR L35 OR (L30 OR L31))
L89          11 SEA SPE=ON  ABB=ON  PLU=ON  L88 AND L85
L90         591 SEA SPE=ON  ABB=ON  PLU=ON  L88 AND (L84 OR (L14 OR L15))
L91         524 SEA SPE=ON  ABB=ON  PLU=ON  L90 AND (L85 OR L16 OR L22 OR (L33
                OR L34))
                D TRI 1-4
L92           5 SEA SPE=ON  ABB=ON  PLU=ON  L91 AND (L30 OR L31)
                D TRI 1-5
L93         122 SEA SPE=ON  ABB=ON  PLU=ON  L91 AND L35
L94          30 SEA SPE=ON  ABB=ON  PLU=ON  L87 OR L89 OR L92
L95           6 SEA SPE=ON  ABB=ON  PLU=ON  L93 AND L94
                D TRI 1-6
L96           1 SEA SPE=ON  ABB=ON  PLU=ON  L95 AND (L6 OR L7 OR L8 OR L9 OR
                L10 OR L11 OR L12)
                D TRI
                D BIB
L97           5 SEA SPE=ON  ABB=ON  PLU=ON  L95 NOT L96

     FILE 'STNGUIDE' ENTERED AT 12:55:26 ON 11 SEP 2009

     FILE 'EMBASE' ENTERED AT 12:57:14 ON 11 SEP 2009
                E GWT1/CT
L98             QUE SPE=ON  ABB=ON  PLU=ON  "GWT1 GENE"+PFT,OLD,NEW,NT/CT
L99           1 SEA SPE=ON  ABB=ON  PLU=ON  L43 OR L98
                E SACCHAROMYC/CT
                E SACCHAROMYCES CER/CT
                E E162+ALL
L100            QUE SPE=ON  ABB=ON  PLU=ON  "SACCHAROMYCES CEREVISIAE PROTEIN"+
                PFT,OLD,NEW,NT/CT
L101          5 SEA SPE=ON  ABB=ON  PLU=ON  GWT1 OR (GWT(1W)(1 OR I)) OR GWTI
L102       1013 SEA SPE=ON  ABB=ON  PLU=ON  (L100 OR L21) AND ((L24 OR L25) OR
                L29)
L103       1015 SEA SPE=ON  ABB=ON  PLU=ON  L99 OR (L101 OR L102)
                E ANTIFUNGAL ACT/CT
                E E181+ALL
L104            QUE SPE=ON  ABB=ON  PLU=ON  "ANTIFUNGAL ACTIVITY"+PFT,OLD,NEW,N
                T/CT
L105            QUE SPE=ON  ABB=ON  PLU=ON  "ANTIFUNGAL AGENT"+PFT,OLD,NEW,NT/C
                T
                E SCREENING/CT
                E E201+ALL
                E E227+ALL
L106            QUE SPE=ON  ABB=ON  PLU=ON  "DRUG SCREENING"+PFT,OLD,NEW,NT/CT

L107         674 SEA SPE=ON  ABB=ON  PLU=ON  L103 AND (L106 OR L16 OR L22 OR
                (L33 OR L34))
L108         263 SEA SPE=ON  ABB=ON  PLU=ON  L107 AND ((L14 OR L15) OR (L104 OR
                L105))
                D TRI 1-3
L109          28 SEA SPE=ON  ABB=ON  PLU=ON  L108 AND ((L104 OR L105) OR L15)
                D TRI 10-12
L110          28 SEA SPE=ON  ABB=ON  PLU=ON  L109 AND (L13 OR L14 OR L15 OR L16
                OR L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR L24 OR L25
                OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33 OR L34
                OR L35)
L111          28 SEA SPE=ON  ABB=ON  PLU=ON  (L109 OR L110)
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L112          2 SEA SPE=ON  ABB=ON  PLU=ON  L111 AND (L6 OR L7 OR L8 OR L9 OR
                L10 OR L11 OR L12)
L113         26 SEA SPE=ON  ABB=ON  PLU=ON  L111 NOT L112

     FILE 'STNGUIDE' ENTERED AT 13:04:57 ON 11 SEP 2009

     FILE 'BIOTECHNO' ENTERED AT 13:06:25 ON 11 SEP 2009

     FILE 'STNGUIDE' ENTERED AT 13:06:52 ON 11 SEP 2009

     FILE 'BIOSIS, CABA, BIOTECHNO, DRUGU, VETU' ENTERED AT 13:07:01 ON 11 SEP
     2009
L114          0 SEA SPE=ON  ABB=ON  PLU=ON  L43
L115         16 SEA SPE=ON  ABB=ON  PLU=ON  L19
L116       2297 SEA SPE=ON  ABB=ON  PLU=ON  L21 AND ((L24 OR L25) OR L29)
L117       2306 SEA SPE=ON  ABB=ON  PLU=ON  (L114 OR L115 OR L116)
L118       1418 SEA SPE=ON  ABB=ON  PLU=ON  L117 AND (L16 OR L22 OR (L33 OR
                L34))
L119         54 SEA SPE=ON  ABB=ON  PLU=ON  L118 AND (L15 OR (L13(5A) L14))
L120          6 SEA SPE=ON  ABB=ON  PLU=ON  L119 AND (L33 OR L34)
L121          6 SEA SPE=ON  ABB=ON  PLU=ON  L119 AND ((L16 OR L22)(7A)(L15 OR
                (L13(5A) L14)))
L122         12 SEA SPE=ON  ABB=ON  PLU=ON  L120 OR L121
                D SCAN
L123         12 SEA SPE=ON  ABB=ON  PLU=ON  L122 AND (L13 OR L14 OR L15 OR L16
                OR L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR L24 OR L25
                OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33 OR L34
                OR L35)
L124         12 SEA SPE=ON  ABB=ON  PLU=ON  (L122 OR L123)
L125          0 SEA SPE=ON  ABB=ON  PLU=ON  L124 AND (L6 OR L7 OR L8 OR L9 OR
                L10 OR L11 OR L12)
L126         12 SEA SPE=ON  ABB=ON  PLU=ON  L124 NOT L125

     FILE 'STNGUIDE' ENTERED AT 13:14:43 ON 11 SEP 2009

     FILE 'PASCAL, JAPIO, LIFESCI, CEABA-VTB, BIOENG, BIOTECHDS, DRUGB, VETB,
     SCISEARCH, CONFSCI, DISSABS, RDISCLOSURE' ENTERED AT 13:15:09 ON 11 SEP
     2009
L127         21 SEA SPE=ON  ABB=ON  PLU=ON  L19
L128        588 SEA SPE=ON  ABB=ON  PLU=ON  (L21(10A)((L24 OR L25) OR L29))
L129      29842 SEA SPE=ON  ABB=ON  PLU=ON  (L16 OR L22)(10A)((L13(5A) L14) OR
                L15)
L130         30 SEA SPE=ON  ABB=ON  PLU=ON  (L127 OR L128) AND (L129 OR (L33
                OR L34))
L131          4 SEA SPE=ON  ABB=ON  PLU=ON  L130 AND (L6 OR L7 OR L8 OR L9 OR
                L10 OR L11 OR L12)
                D SCAN
L132         26 SEA SPE=ON  ABB=ON  PLU=ON  L130 NOT L131

     FILE 'STNGUIDE' ENTERED AT 13:21:45 ON 11 SEP 2009
                D QUE L43
                D QUE L63
                D QUE L79
                D QUE L97
                D QUE L113
                D QUE L126
                D QUE L132

     FILE 'HCAPLUS, WPIX, MEDLINE, EMBASE, BIOSIS, CABA, BIOTECHNO, DRUGU,
     LIFESCI, BIOENG, BIOTECHDS, SCISEARCH, DISSABS' ENTERED AT 13:23:51 ON 11
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     SEP 2009
L133         67 DUP REM L63 L79 L97 L113 L126 L132 (15 DUPLICATES REMOVED)
                    ANSWERS '1-7' FROM FILE HCAPLUS
                    ANSWERS '8-12' FROM FILE WPIX
                    ANSWERS '13-17' FROM FILE MEDLINE
                    ANSWERS '18-42' FROM FILE EMBASE
                    ANSWERS '43-44' FROM FILE DRUGU
                    ANSWERS '45-49' FROM FILE LIFESCI
                    ANSWERS '50-51' FROM FILE BIOTECHDS
                    ANSWERS '52-60' FROM FILE SCISEARCH
                    ANSWERS '61-67' FROM FILE DISSABS
                SAVE TEMP L133 ARC935MAINP/A

     FILE 'STNGUIDE' ENTERED AT 13:24:16 ON 11 SEP 2009

     FILE 'HCAPLUS, WPIX, MEDLINE, EMBASE, DRUGU, LIFESCI, BIOTECHDS,
     SCISEARCH, DISSABS' ENTERED AT 13:24:51 ON 11 SEP 2009
                D QUE L64
L*** DEL       7 S L61 NOT L62
L*** DEL       6 S L77 NOT L78
L*** DEL       5 S L95 NOT L96
L*** DEL      26 S L111 NOT L112
L*** DEL       2 S L124 NOT L125
L*** DEL       5 S L130 NOT L131
L*** DEL       3 S L130 NOT L131
L*** DEL      10 S L130 NOT L131
L*** DEL       7 S L130 NOT L131
L134         38 SEA SPE=ON  ABB=ON  PLU=ON  L133 AND L64
L135         38 DUP REM L134 (0 DUPLICATES REMOVED)
                    ANSWERS '1-2' FROM FILE HCAPLUS
                    ANSWERS '3-4' FROM FILE WPIX
                    ANSWERS '5-18' FROM FILE EMBASE
                    ANSWERS '19-20' FROM FILE DRUGU
                    ANSWERS '21-23' FROM FILE LIFESCI
                    ANSWERS '24-25' FROM FILE BIOTECHDS
                    ANSWERS '26-33' FROM FILE SCISEARCH
                    ANSWERS '34-38' FROM FILE DISSABS

     FILE 'STNGUIDE' ENTERED AT 13:26:30 ON 11 SEP 2009

     FILE 'HCAPLUS, WPIX, EMBASE, DRUGU, LIFESCI, BIOTECHDS, SCISEARCH,
     DISSABS' ENTERED AT 13:27:04 ON 11 SEP 2009
                D IBIB ED ABS HITIND HITSTR 1-2

     FILE 'STNGUIDE' ENTERED AT 13:27:05 ON 11 SEP 2009

     FILE 'HCAPLUS, WPIX, EMBASE, DRUGU, LIFESCI, BIOTECHDS, SCISEARCH,
     DISSABS' ENTERED AT 13:28:08 ON 11 SEP 2009
                D IFULL 3-4

     FILE 'STNGUIDE' ENTERED AT 13:28:09 ON 11 SEP 2009

     FILE 'HCAPLUS, WPIX, EMBASE, DRUGU, LIFESCI, BIOTECHDS, SCISEARCH,
     DISSABS' ENTERED AT 13:29:01 ON 11 SEP 2009
                D BIB ED AB IND 5-38

     FILE 'STNGUIDE' ENTERED AT 13:29:04 ON 11 SEP 2009
                D QUE L62
                D QUE L78
                D QUE L96
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               D QUE L112
               D QUE L125
               D QUE L131

     FILE 'HCAPLUS, WPIX, MEDLINE, EMBASE, JAPIO, BIOTECHDS' ENTERED AT
     13:35:30 ON 11 SEP 2009
L136         10 DUP REM L62 L78 L96 L112 L125 L131 (8 DUPLICATES REMOVED)
                    ANSWERS '1-5' FROM FILE HCAPLUS
                    ANSWERS '6-8' FROM FILE WPIX
                    ANSWER '9' FROM FILE MEDLINE
                    ANSWER '10' FROM FILE JAPIO
               SAVE TEMP L136 ARC935INV/A

     FILE 'STNGUIDE' ENTERED AT 13:35:44 ON 11 SEP 2009

     FILE 'HCAPLUS, WPIX, MEDLINE, JAPIO' ENTERED AT 13:36:06 ON 11 SEP 2009
               D IBIB ED ABS HITIND HITSTR 1-5

     FILE 'STNGUIDE' ENTERED AT 13:36:10 ON 11 SEP 2009

     FILE 'HCAPLUS, WPIX, MEDLINE, JAPIO' ENTERED AT 13:36:27 ON 11 SEP 2009
               D IFULL 6-8

     FILE 'STNGUIDE' ENTERED AT 13:36:29 ON 11 SEP 2009

     FILE 'HCAPLUS, WPIX, MEDLINE, JAPIO' ENTERED AT 13:36:55 ON 11 SEP 2009
               D BIB ED AB IND 9-10

     FILE 'STNGUIDE' ENTERED AT 13:36:56 ON 11 SEP 2009

     FILE 'STNGUIDE' ENTERED AT 13:37:06 ON 11 SEP 2009


     FILE HOME

     FILE STNGUIDE
     FILE CONTAINS CURRENT INFORMATION.
     LAST RELOADED: Sep  4, 2009 (20090904/UP).

     FILE ZCAPLUS

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FILE HCAPLUS

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FILE LAST UPDATED: 10 Sep 2009 (20090910/ED)
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FILE WPIX
FILE LAST UPDATED: 7 SEP 2009 <20090907/UP>
MOST RECENT UPDATE: 200957 <200957/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE
>>> Now containing more than 1.4 million chemical structures in DCR <<<

>>> IPC, ECLA, US National Classifications and Japanese F-Terms
and FI-Terms have been updated with reclassifications to
mid-June 2009.
No update date (UP) has been created for the reclassified
documents, but they can be identified by
specific update codes (see HELP CLA for details)<<<

FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:

http://www.stn-international.com/stn_guide.html

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomsonreuters.com/support/patents/coverage/latestupdate

EXPLORE DERWENT WORLD PATENTS INDEX IN STN ANAVIST, VERSION 2.0:
http://www.stn-international.com/DWPIAnaVist2_0608.html

>>> HELP for European Patent Classifications see HELP ECLA, HELP ICO <<<

Manual Code Revision
Thomson Reuters is asking for customer input for the 2010 manual code revision of the Electrical Patents Index (EPI) and Chemical Patents Index (CPI) Manual Codes. Read more at
http://go.thomsonreuters.com/dwpi_code-revision

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 9 SEP 2009 HIGHEST RN 1181864-71-0
DICTIONARY FILE UPDATES: 9 SEP 2009 HIGHEST RN 1181864-71-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

FILE MEDLINE
FILE LAST UPDATED: 10 Sep 2009 (20090910/UP). FILE COVERS 1949 TO DATE.

MEDLINE and LMEDLINE have been updated with the 2009 Medical Subject Headings (MeSH) vocabulary and tree numbers from the U.S. National Libra of Medicine (NLM). Additional information is available at

http://www.nlm.nih.gov/pubs/techbull/nd08/nd08_medline_data_changes_2009.

On February 21, 2009, MEDLINE was reloaded. See HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

See HELP RANGE before carrying out any RANGE search.

FILE EMBASE
FILE COVERS 1974 TO 11 Sep 2009 (20090911/ED)

EMBASE was reloaded on March 30, 2008.

EMBASE is now updated daily. SDI frequency remains weekly (default)

and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

Beginning January 2008, Elsevier will no longer provide EMTREE codes as part of the EMTREE thesaurus in EMBASE. Please update your current-awareness alerts (SDIs) if they contain EMTREE codes.

For further assistance, please contact your local helpdesk.

FILE BIOTECHNO
FILE LAST UPDATED: 7 JAN 2004 <20040107/UP>
FILE COVERS 1980 TO 2003.
THIS FILE IS A STATIC FILE WITH NO UPDATES

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN /CT AND BASIC INDEX <<<

FILE BIOSIS
FILE COVERS 1926 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 10 September 2009 (20090910/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926 through 1968. These records have been re-indexed to match current BIOSIS indexing.

FILE CABA
FILE COVERS 1973 TO 3 Sep 2009 (20090903/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

The CABA file was reloaded 7 December 2003. Enter HELP RLOAD for details.

FILE DRUGU
FILE LAST UPDATED: 9 SEP 2009 <20090909/UP>
>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<
>>> THESAURUS AVAILABLE IN /CT <<<

FILE VETU
FILE LAST UPDATED: 2 JAN 2002 <20020102/UP>
FILE COVERS 1983-2001

FILE PASCAL
FILE LAST UPDATED: 7 SEP 2009 <20090907/UP>
FILE COVERS 1977 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE IN THE BASIC INDEX (/BI) FIELD <<<

FILE JAPIO

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FILE LAST UPDATED:            28 AUG 2009       <20090828/UP>
MOST RECENT PUBLICATION DATE: 28 MAY 2009       <20090528/PD>
>>> GRAPHIC IMAGES AVAILABLE <<<

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION (SLART) IS AVAILABLE
    IN THE BASIC INDEX (/BI) FIELD <<<

FILE LIFESCI
FILE COVERS 1978 TO 9 Sep 2009 (20090909/ED)

FILE CEABA-VTB
FILE LAST UPDATED: 25 AUG 2009       <20090825/UP>
FILE COVERS 1966 TO DATE

>>> DECHEMA, the producer of CEABA-VTB is using a new classification
    scheme.
    The new classification schemes are available as a PDF file
    and may be downloaded free-of-charge from:
    http://www.stn-international.com/cc-de.html
    and
    http://www.stn-international.com/cc-en.html<<<

FILE BIOENG
FILE LAST UPDATED: 13 AUG 2009       <20090813/UP>
FILE COVERS 1982 TO DATE

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
    THE BASIC INDEX <<<

FILE BIOTECHDS
FILE LAST UPDATED: 7 SEP 2009       <20090907/UP>
FILE COVERS 1982 TO DATE

>>> USE OF THIS FILE IS LIMITED TO BIOTECH SUBSCRIBERS <<<


FILE DRUGB
 >>>  FILE COVERS 1964 TO 1982 - CLOSED FILE  <<<


FILE VETB
FILE LAST UPDATED: 25 SEP 94      <940925/UP>
FILE COVERS 1968-1982


FILE SCISEARCH

FILE COVERS 1974 TO 10 Sep 2009 (20090910/ED)

SCISEARCH has been reloaded, see HELP RLOAD for details.

FILE CONFSCI
FILE COVERS 1973 TO 30 Jun 2009 (20090630/ED)

CSA has resumed updates, see NEWS FILE

FILE DISSABS
FILE COVERS 1861 TO 8 SEP 2009 (20090908/ED)

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